Southern Medical Journal

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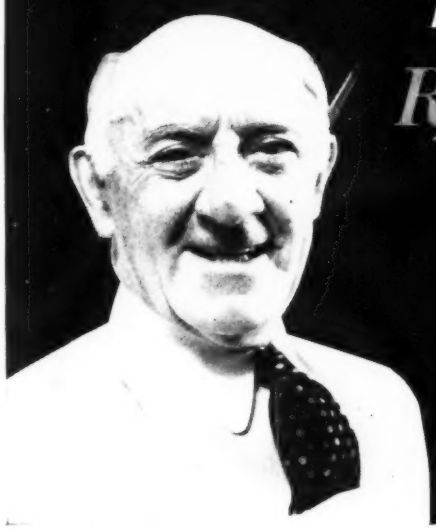

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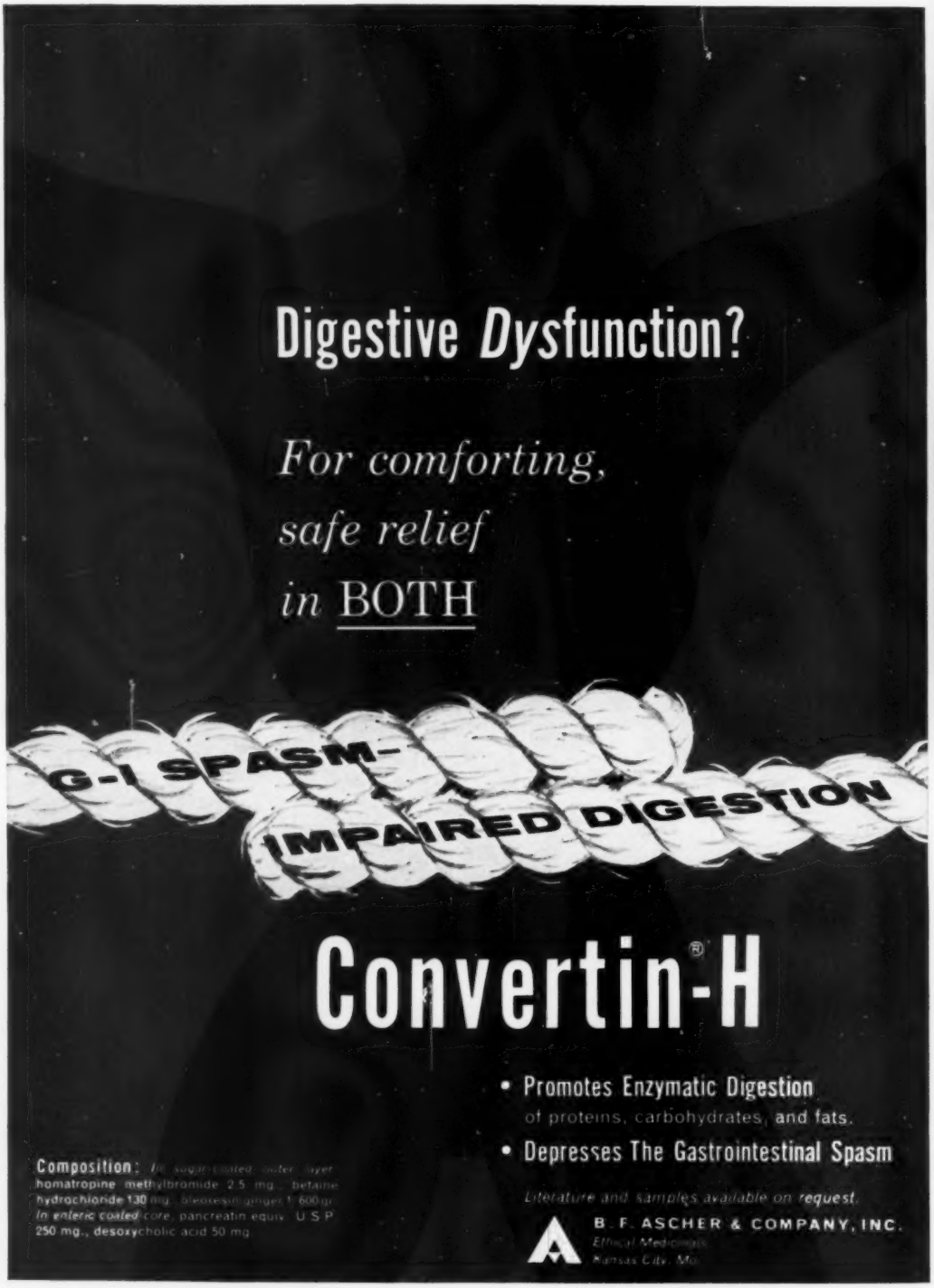
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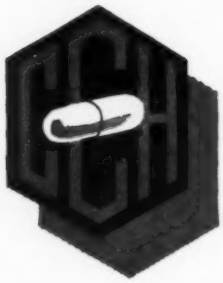

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1. Rein, C. R., Fleischmajer, R., and Rosenthal, A. L.: J. A. M. A. *165*:1821, (Dec. 7) 1957.
2. Shelley, W. B., and Pillsbury, D. M.: Personal Communication.
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12. Cooke, R. A.: Personal Communication.
13. Dubois, E. L.: Personal Communication.

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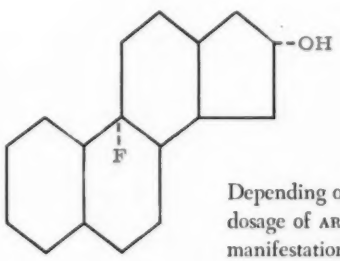

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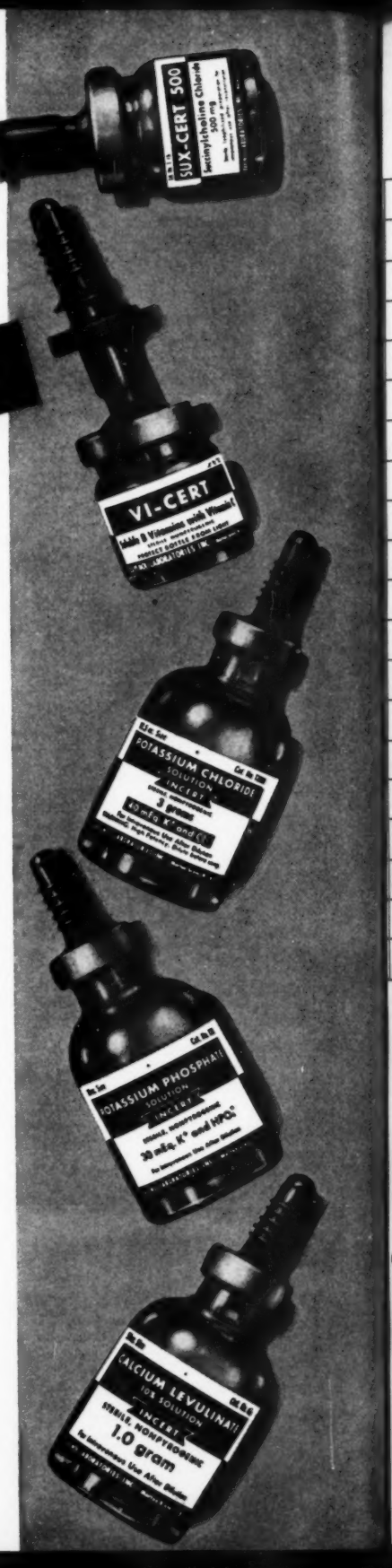

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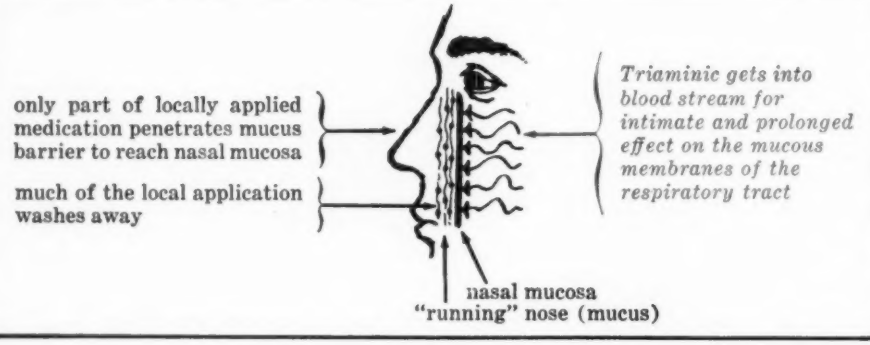
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*Morrison, L. F.: Arch. Otolaryng. 59:48-53 (Jan.) 1954.

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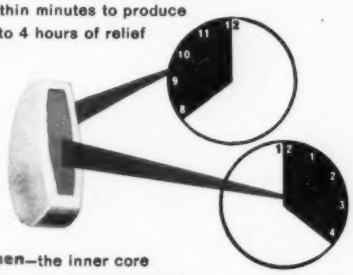

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LOW pH RETENTION

Massengill Powder is buffered to retain an acid condition. In a recent clinical observation, ambulatory patients—with an alkaline vaginal mucosa resulting from pathogens—maintained an acid vaginal mucosa of pH 3.5 for a period of 4 to 6 hours after douching with Massengill Powder; recumbent patients maintained a satisfactory acid condition up to 24 hours. Simple acid douches (vinegar or lactic acid) are quickly neutralized by an alkaline vaginal mucosa; therefore, they are somewhat unsatisfactory in maintaining the required acid pH of the vagina.[2]

LOWER SURFACE TENSION

Massengill Powder in the standard solution has a surface tension of 50 dynes/cm. as compared to that of water and simple acid solutions with 72 dynes/cm. This added property of reduced surface tension enables Massengill Powder to penetrate into and cleanse the folds of the vaginal mucosa, thus increasing the therapeutic effectiveness. Lowered surface tension makes the cell wall and cytoplasmic membrane of the infecting organism more permeable and thus more susceptible to specific therapy.[2]

SUPPLY

Massengill Powder is supplied in glass jars of the following sizes:

Small, 3 oz.
Medium, 6 oz.
Large, 16 oz.
Hospital Size, 5 lbs.

Pads of douching instructions for patient use available on request.

REFERENCES

1. Lang, W.R., Rakoff, A.E., Am. Geriatrics Soc. *1*:520 (1953).
2. Arnot, P.H., The Problem of Douching, Western Journal of Surg., Obs., and Gyn., Vol. 62, No. *2*:85 (1954).

The S. E. MASSENGILL Company BRISTOL, TENNESSEE
NEW YORK SAN FRANCISCO KANSAS CITY

the chill

the cough

the aching muscles

the fever

Viral upper respiratory infection. . . . For this patient, your management will be twofold—prompt symptomatic relief plus the prevention and treatment of bacterial complications. PEN·VEE·*Cidin* backs your attack by broad, multiple action. It relieves aches and pains, and reduces fever. It counters depression and fatigue. It alleviates cough. It calms the emotional unrest. And it dependably combats bacterial invasion because it is the only preparation of its kind to contain penicillin V.

SUPPLIED: Capsules, bottles of 36. Each capsule contains 62.5 mg. (100,000 units) of penicillin V, 194 mg. of salicylamide, 6.25 mg. of promethazine hydrochloride, 130 mg. of phenacetin, and 3 mg. of mephentermine sulfate.

This advertisement conforms to the Code for Advertising of the Physicians' Council for Information on Child Health.

PEN·VEE·*Cidin*®

Penicillin V with Salicylamide, Promethazine Hydrochloride, Phenacetin, and Mephentermine Sulfate, Wyeth

Wyeth

Philadelphia 1, Pa.

GET YOUR BABIES OFF TO A STRONG START WITH

Baker's

MODIFIED MILK

A complete formula in liquid and powder form prepared exclusively from Grade A Milk

Happy Jeanette, aglow with health, is a Baker's Blue Ribbon Baby.

Doctor, your dietary decision can build *Blue Ribbon* babies. The baby who wins the blue ribbon is the one whose doctor—no one else—selects its formula.

BAKER'S MODIFIED MILK BUILDS BLUE RIBBON BABIES

- A complete, balanced uniform formula.
- Convenient and easy to prepare—simply add water.
- Made from milk of outstanding purity.
- Provides adequate amounts of all known essential vitamins plus much-needed iron.
- Butterfat replaced by easily digested vegetable oils.
- Twice homogenized for better digestion and absorption.
- Helps doctor control infant's formula longer. Advertised to the medical profession only.
- Economical to use—eliminates need for additional vitamins and iron.

FURNISHED GRATIS TO HOSPITALS FOR NURSERY USE

Available in drug stores

OTHER PRODUCTS—VARAMEL—a scientifically formulated evaporated milk product prepared exclusively from Grade A Milk

Normal Dilutions
Liquid Form—1 fl. oz. milk to 1 fl. oz. water
Powder Form—1 Tbsp. powder to 2 fl. oz. water
20 calories per ounce

The Baker Laboratories, Inc. • Cleveland 3, Ohio

Milk Products Exclusively for the Medical Profession

in pyelonephritis delay is dangerous...

FURADANTIN® *first*...

BRAND OF NITROFURANTOIN

for rapid eradication of infection

In the majority of 112 cases of acute, persistent or relapsing urinary tract infections "nitrofurantoin [FURADANTIN] was effective clinically, with a pronounced improvement, indicated by the appearance of the urine as well as by verbal commendation by the patient, within 24 to 36 hours . . . Some of these patients with seemingly impossible cases were cured of their infection."*

FURADANTIN *first* because of these advantages: a specific for urinary tract infections • rapid bactericidal action • negligible development of bacterial resistance • nontoxic to kidneys, liver and blood-forming organs.

AVERAGE DOSAGE: *ADULTS*—four 100 mg. tablets daily; 1 tablet during each meal and 1 on retiring, with food or milk. In acute, uncomplicated infections, 50 mg. q.i.d. may be prescribed. If patient is unresponsive after 2 to 3 days, increase dose to 100 mg. q.i.d.

CHILDREN—5 to 7 mg. per Kg. (2.2 to 3.1 mg. per lb.) per 24 hours.

SUPPLIED: Tablets, 50 and 100 mg. Oral Suspension (25 mg. per 5 cc. tsp.).

*Stewart, B. L., and Rowe, H. J.: J. Am. M. Ass. 160:1221, 1956.

EATON LABORATORIES, NORWICH, NEW YORK

Nitrofurans—a new class of antimicrobials—neither antibiotics nor sulfonamides

new
improved
formula!

THERAGRAN

Squibb Vitamins for Therapy

expanded to include certain essential vitamins
extra value...
at no extra cost to your patients

Theragran—the original and most widely prescribed therapeutic vitamin preparation—is now expanded to provide additional nutritional support for your adult patients. In keeping with the proposals of investigators, such vitamins as B_{12}, pyridoxine and d-calcium pantothenate have been added to the formula, and the ascorbic acid content has been increased. These improvements in the Theragran formula provide your patients with extra value at no additional cost.

Each new, improved Theragran capsule supplies:

Vitamin A	25,000 U.S.P. Units
Vitamin D	1,000 U.S.P. Units
Thiamine Mononitrate	10 mg.
Riboflavin	10 mg.
Niacinamide	100 mg.
Ascorbic Acid	200 mg.
Pyridoxine Hydrochloride	5 mg.
d-Calcium Pantothenate	20 mg.
Vitamin B_{12} activity concentrate	5 mcg.

1 or more capsules daily as recommended by a physician.
Family Pack of 180. Bottles of 30, 60, 100 and 1000.

ALSO AVAILABLE

new! **THERAGRAN JUNIOR**
formulated for vitamin therapy in children and adolescents as Theragran is formulated for adults.

THERAGRAN LIQUID
for patients who prefer liquid vitamin therapy

THERAGRAN-M
with extra vitamins and minerals

"THERAGRAN" IS A SQUIBB TRADEMARK

SQUIBB

Squibb Quality—
the Priceless
Ingredient

"THERAGRAN" IS A SQUIBB TRADEMARK

ACHROCIDIN*

TETRACYCLINE-ANTIHISTAMINE-ANALGESIC COMPOUND LEDERLE

A versatile, well-balanced formula offering in one tablet the drugs often prescribed separately for treating upper respiratory infections.

Traditional and nonspecific nasopharyngeal symptoms of malaise and chilly sensations are rapidly relieved, and headache, muscular pain, and pharyngeal and nasal discharges are reduced or eliminated.

Early effective therapy is provided against such bacterial complications as sinusitis, otitis, bronchitis and pneumonitis to which the patient may be highly vulnerable at this time.

Adult dosage for ACHROCIDIN Tablets and new, caffeine-free ACHROCIDIN Syrup is two tablets or teaspoonfuls of syrup three or four times daily. Dosage for children reduced according to weight and age.

Available on prescription only.

TABLETS *(Sugar-coated)*
Each tablet contains:

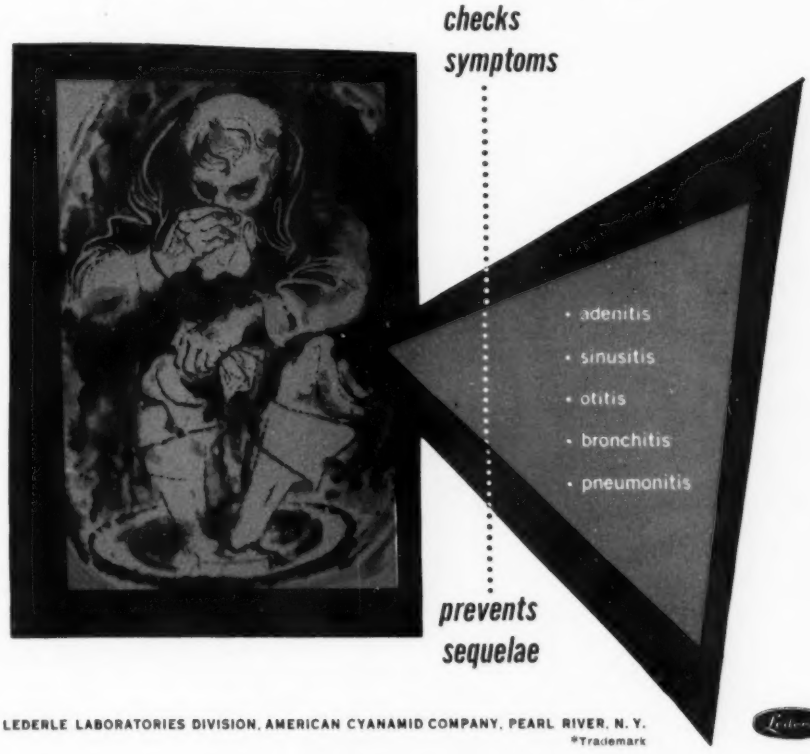
ACHROMYCIN® Tetracycline	125 mg.
Phenacetin	120 mg.
Caffeine	30 mg.
Salicylamide	150 mg.
Chlorothen Citrate	25 mg.

Bottles of 24 and 100

SYRUP *(Lemon-lime flavored)*
Each teaspoonful (5 cc.) contains:

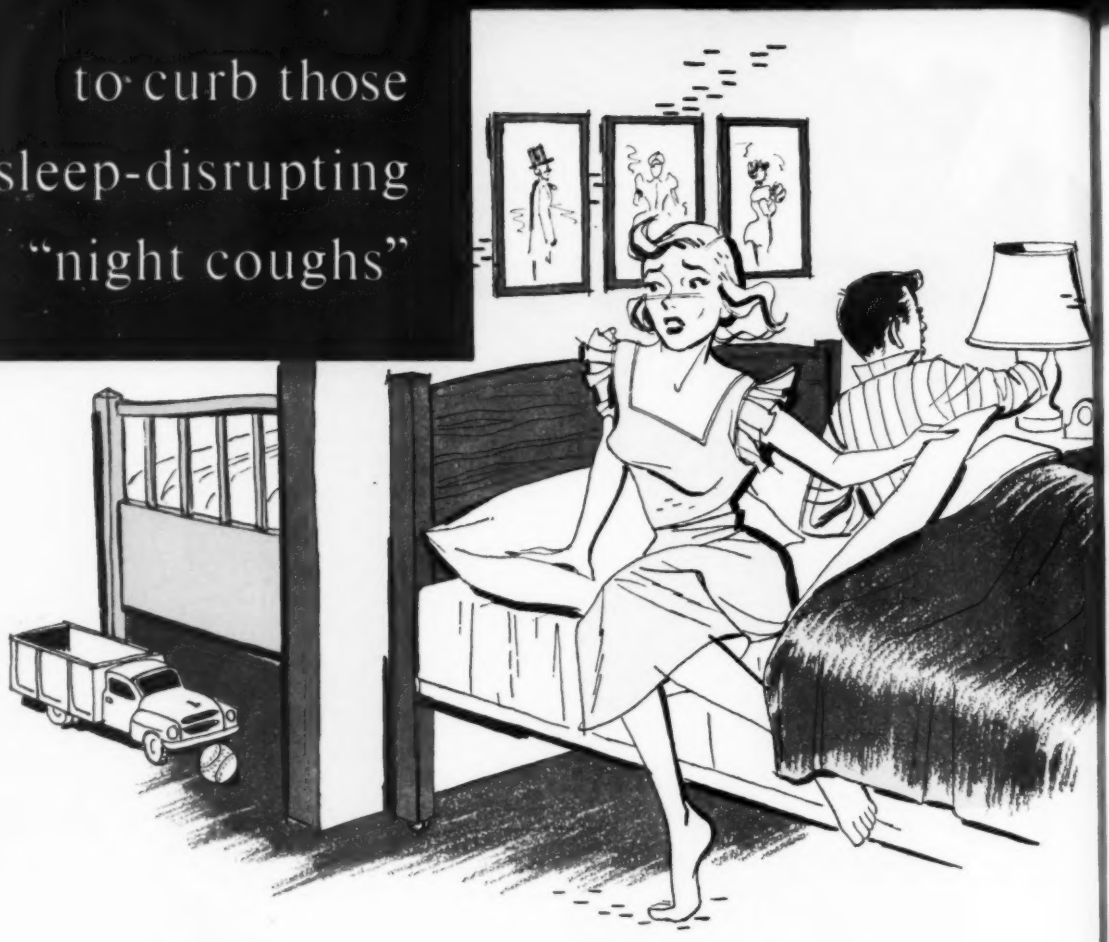
ACHROMYCIN® Tetracycline equivalent to tetracycline HCl	125 mg.
Phenacetin	120 mg.
Salicylamide	150 mg.
Ascorbic Acid (C)	25 mg.
Pyrilamine Maleate	15 mg.
Methylparaben	4 mg.
Propylparaben	1 mg.

Bottle of 4 oz.



LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, N. Y.
*Trademark

to curb those sleep-disrupting "night coughs"



that waken the whole household...

CLISTIN® EXPECTORANT

Clistin Expectorant is the only cough product containing CLISTIN Carbinoxamine Maleate—that well-accepted, potent antihistamine. Relieves coughs of the common cold and coughs of allergic or non-allergic upper respiratory conditions.

Clistin Expectorant—samples on request

McNEIL
LABORATORIES, INC.
Philadelphia 32, Pa.

"anti-cough"...

antihistaminic...

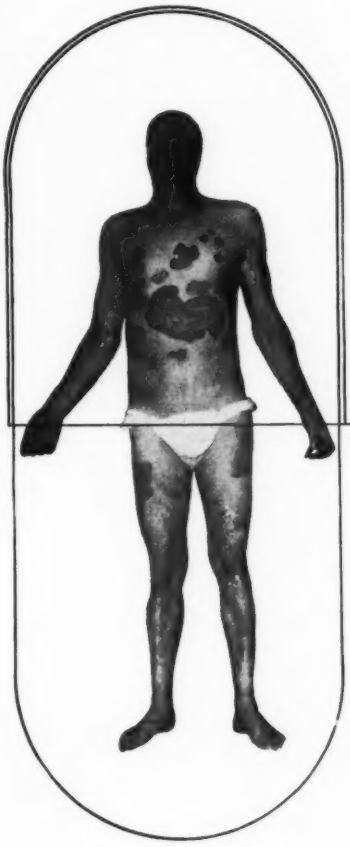
completely safe for pediatric use...

non-narcotic...

does not upset the stomach...

tastes wonderful

PSORIASIS



Proved Clinically Effective Oral Therapy—

maintenance regimen may keep patients lesion-free.

COMPLETE LITERATURE AND REPRINTS
UPON REQUEST. JUST SEND AN Rx BLANK.

LIPAN®

Spirt & Co., Inc.
WATERBURY, CONN.

LIPAN Capsules contain: Specially prepared highly activated, desiccated and defatted *whole* Pancreas: Thiamin HCl, 1.5 mg. Vitamin D, 500 I.U.

Available: Bottles 180's, 500's.

©Copyright 1956 Spirt & Co.

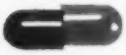
where there's a cold
there's

CORICIDIN

when it's a simple cold

CORICIDIN® TABLETS

when it's an all-over cold



CORICIDIN FORTE
CAPSULES

when infection threatens the cold

CORICIDIN with PENICILLIN
TABLETS

when pain is a dominating factor

CORICIDIN with CODEINE
(gr. ¼ or gr. ½) TABLETS◊

when children catch cold

CORICIDIN MEDILETS®

when cough marks the cold

CORICIDIN SYRUP○

◊ Narcotic for which oral Rx is permitted
○ Exempt narcotic

SCHERING CORPORATION · BLOOMFIELD, NEW JERSEY

CN-J-228

Schering

don't let them broadcast colds

turn
off
the
cough
with

CORICIDIN

monitors the cough *and* the cold in children and adults

colds and fever take flight like magic

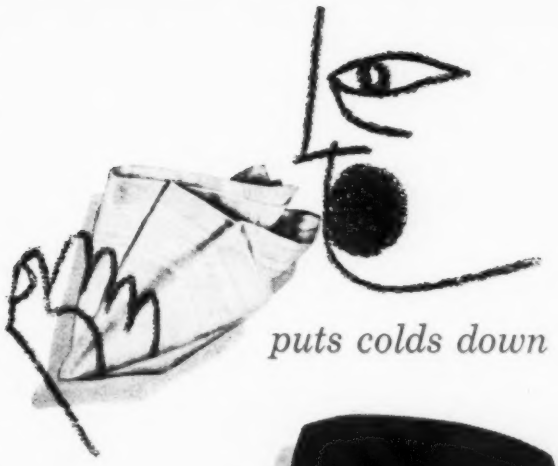
with

CORICIDIN® MEDILETS®

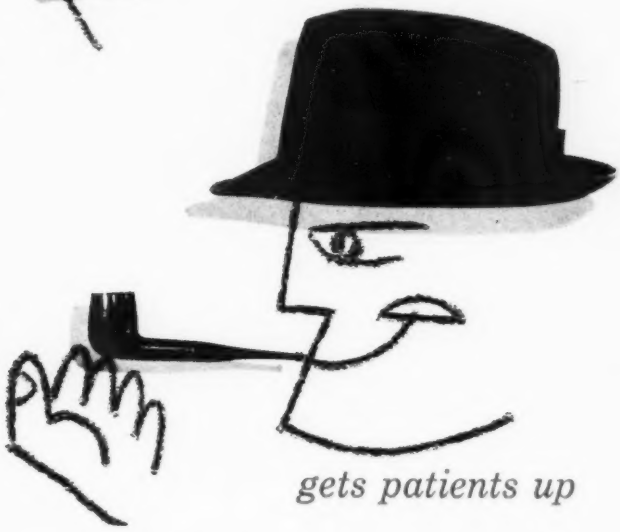
(no caffeine)

color-flecked tablets for relief of sneezes, sniffles, congestion and fever of children's colds

Schering SCHERING CORPORATION • BLOOMFIELD, NEW JERSEY CN-J-428



puts colds down



gets patients up

CORICIDIN FORTE

on Rx only

CAPSULES

for "get-up-and-go"
METHAMPHETAMINE

• buoys spirits • potentiates pain relief • aids decongestive action

for stress support VITAMIN C

• supplements illness requirements • bolsters resistance to infection

for extra relief ANTIHISTAMINE

• higher dosage strength • optimal therapeutic benefit • virtually no side effects

Each red and yellow CORICIDIN FORTE Capsule provides:

CHLOR-TRIMETON® Maleate (chlorprophenpyridamine maleate)	4 mg.
Salicylamide	0.19 Gm.
Phenacetin	0.13 Gm.
Caffeine	30 mg.
Ascorbic acid	50 mg.
Methamphetamine hydrochloride	1.25 mg.

On Rx and cannot be refilled without your permission

dosage

One capsule every four to six hours.

packaging

Bottles of 100 and 1000.

CORICIDIN,® brand of analgesic-antipyretic.

SCHERING CORPORATION • BLOOMFIELD, NEW JERSEY

Schering

CN-J-328

NOW

COUNTERACT DEPRESSED MOODS *without stimulation*

- Relieves depression without euphoria —*not a stimulant*
- Restores natural sleep without depressive aftereffects —*not a hypnotic*

- Rapid onset of action
- Side effects are minimal and easily controlled

▲Deprol▲

Composition: Each tablet contains 400 mg. meprobamate and 1 mg. benactyzine HCl

Average Adult Dose: 1 tablet q.i.d.

WALLACE LABORATORIES, *New Brunswick, N. J.*

Literature and samples on request

CD-6167

designed

for

control of

diarrhea

AND
RELIEF OF INFLAMMATIONS
AND ACUTE UPSETS OF THE
GASTROINTESTINAL TRACT

RHEASTAT

Each fluidounce contains:

PHENOBARBITAL	¼ gr. (16.2 mg.)
HYOSCYAMINE SULFATE	0.1286 mg.
ATROPINE SULFATE	0.0250 mg.
HYOSCINE HYDROBROMIDE	0.0074 mg.

Sedative and Antispasmodic

KAOLIN, COLLOIDAL	90 gr. (6 Gm.)
PECTIN	5 gr. (0.32 Gm.)

Adsorbent and Detoxicant

SODIUM	6 mEq.
POTASSIUM	4 mEq.

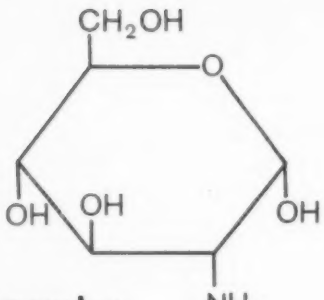
Ion Replacement

IN A SPECIAL ALUMINUM HYDROXIDE GEL

Antacid

USUAL ADULT DOSE
1 OR 2 TABLESPOONFULS
EVERY 3 OR 4 HOURS

VANPELT & BROWN, INC. Richmond 4, Va.



Glucosamine ... a physiologic absorption-enhancing agent

In the search for the ideal antibiotic-enhancement agent, Pfizer had three requirements to fill: (1) the adjuvant had to produce significantly higher antibiotic blood levels, (2) it had to achieve these higher blood levels consistently from patient to patient, (3) the adjuvant itself had to be perfectly safe to use.

Enhancement studies involving 84 adjuvants (including sorbitol, citric acid, sodium hexametaphosphate, and other organic acids and chelating agents, as well as phosphate complex and other analogs), and 30,000 blood level determinations revealed glucosamine as the enhancement agent of choice. Not only did glucosamine considerably increase antibiotic blood levels, but it produced these higher blood levels more consistently in crossover tests. And, importantly, glucosamine has no adverse effect in the human body.

Glucosamine is a normal physiologic metabolite that is found widely in the human body. Glucosamine does not irritate the gastrointestinal tract; it is sodium free and releases only four calories of energy per gram. Further, there is evidence that glucosamine may influence favorably the bacterial flora of the intestine.

faster absorptio higher tetra- cycline blood levels

new well-tolerated

COSA-T

GLUCOSAMINE-POTENTIATED TETRACYCLINE

Three advantages of
glucosamine-potentiated
tetracycline, for
your consideration

2 3

achieved with
physiologic advantages
of glucosamine a normal human metabolite

greater consistency
of higher tetracycline
blood levels

TETRACYN*

The most widely prescribed broad-spectrum antibiotic now potentiated with glucosamine, the enhancing agent of choice

Capsules, 250 mg., 125 mg.

Half strength (125 mg. capsule) for
long-term indications or pediatric use

Pfizer PFIZER LABORATORIES, *Division, Chas. Pfizer & Co., Inc.*, Brooklyn 6, N. Y.

*Trademark

MARSILID

(iproniazid)

the new psychic energizer

*"a major breakthrough . . . in mental disease"**

Q. What is Marsilid?

A. Marsilid ROCHE (iproniazid) is a psychic energizer – the very opposite of a tranquilizer – of unparalleled value in mild and severe depression. Marsilid is an amine-oxidase inhibitor which affects the metabolism of serotonin, epinephrine, norepinephrine and other amines.

Q. How does Marsilid act?

A. Marsilid restores a feeling of well-being and promotes an increase in appetite, weight and vitality. It restores depleted nervous energy and stimulates appetite and weight gain in chronic debilitating disorders.

Marsilid, in effect, has a protective or sparing action on serotonin and norepinephrine in the brain. When subjects treated with Marsilid take reserpine, the effect of Marsilid is potentiated by reserpine – the opposite of the usual tranquilizing results of reserpine therapy. This is due to the fact that reserpine releases serotonin and norepinephrine from their bound forms in the

*T. R. Robie, paper read at First Marsilid Symposium, New York City, November 29, 1957

brain; normally these substances are rapidly destroyed by amine oxidase.

Q. How soon is the effect of Marsilid apparent?

A. Marsilid is a relatively slow-acting drug; even in mild depression results may not be evident for a week or two. In chronically depressed or regressed psychotics, results may be apparent only after a month or more.

Q. How does Marsilid compare with shock treatment?

A. Marsilid usually obviates the need for shock treatment. The drug has repeatedly been effective in patients who had not responded to shock therapy (both insulin and electroshock).

Q. What is the dosage of Marsilid?

A. Like all potent drugs, Marsilid requires individual dosage adjustment for best results. It is therefore important to follow the dosage directions carefully.

Q. What precautions should be taken with Marsilid?

A. Like cortisone, digitalis and other potent drugs, Marsilid should be used with care and the precautions listed in the literature should be observed.

Q. What is the clinical background for Marsilid?

A. The therapeutic usefulness of Marsilid has been described in over 50 recent publications. For reprints and information on the clinical use of Marsilid, write to Professional Service Department, Roche Laboratories, Nutley 10, New Jersey.

Marsilid® Phosphate — brand of iproniazid phosphate
(1-isonicotinyl-2-isopropylhydrazine phosphate)
Roche — Reg. U. S. Pat. Off.

ROCHE LABORATORIES • *Division of Hoffmann-La Roche Inc* • *Nutley, New Jersey*

when you want Broad-Spectrum Benefits . . .

When you want extended antibacterial coverage with high relative safety, consider PEN·VEE SULFAS. Consider how it permits you to reserve the conventional broad-spectrum antibiotics for the resistant infections specifically requiring them. Consider PEN·VEE SULFAS because it unites penicillin V and sulfapyrimidines for potent complementary action. Prescribe it for wide antimicrobial attack in mixed infections and those not readily diagnosed.

Supplied: PEN·VEE SULFAS Tablets, bottles of 36. Each tablet contains 90 mg. (150,000 units) of penicillin V, 0.25 Gm. of sulfadiazine, and 0.25 Gm. of sulfamerazine. PEN·VEE SULFAS for Suspension, bottles of 2 fl. oz. upon reconstitution. Each 5-cc. teaspoonful after reconstitution contains 90 mg. (150,000 units) of benzathine penicillin V, 0.25 Gm. of sulfadiazine, and 0.25 Gm. of sulfamerazine.

Wyeth®
Philadelphia 1, Pa.

PEN·VEE® SULFAS

Tablets: Penicillin V (Phenoxymethyl Penicillin) and Sulfonamides
For Suspension: Benzathine Penicillin V and Sulfonamides

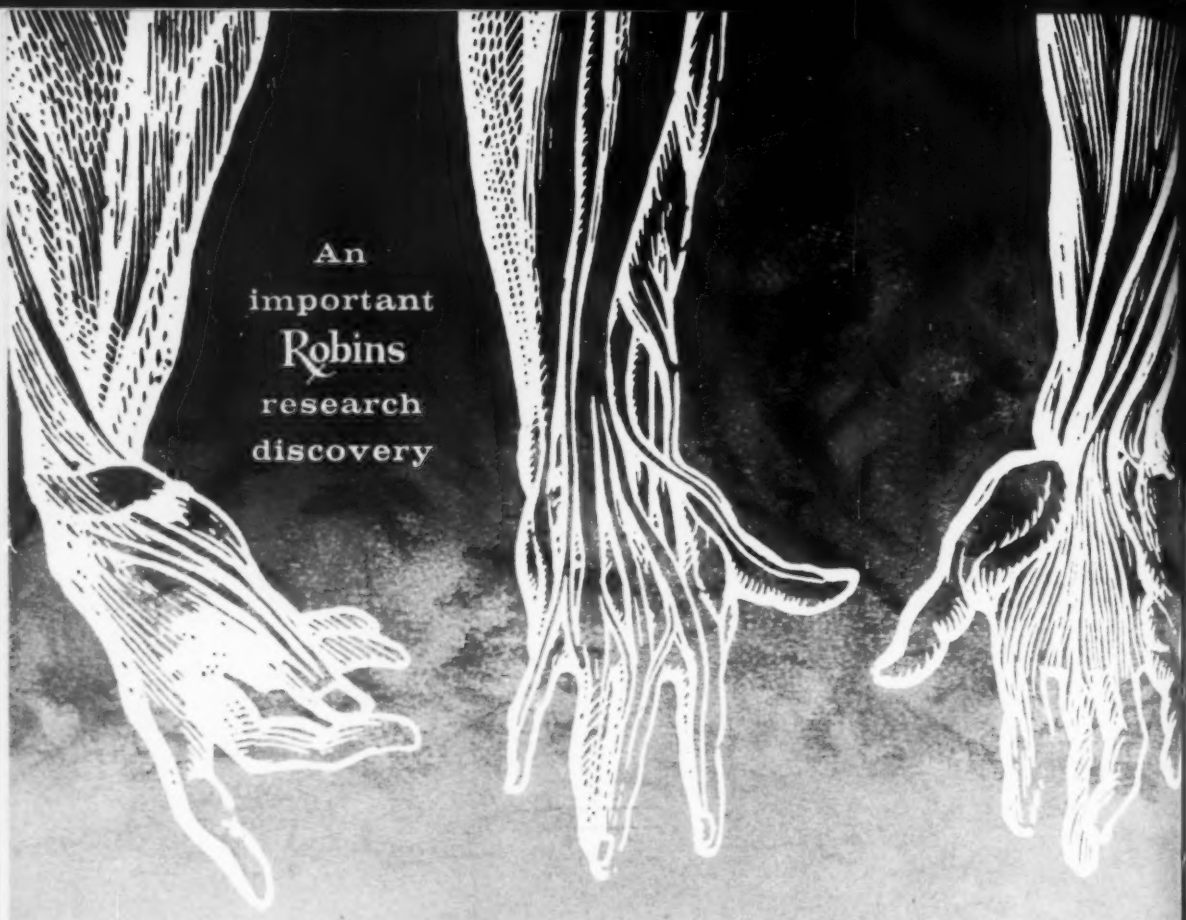
From the Robins *Research Laboratories*

A NEW
HIGHLY EFFICIENT
SKELETAL
MUSCLE RELAXANT

Robaxin

Unique in chemical formulation
and outstanding for

- Sustained relaxing action on skeletal muscle
- Relative freedom from adverse side effects



...remarkable efficiency in skeletal muscle relaxation

Robaxin®

(METHOCARBAMOL ROBINS, U.S. PAT. NO. 2770649)

Selective and specific action

Synthesized in the Robins Research Laboratories and clinically tested by hundreds of physicians, ROBAXIN offers *selective* and *specific* relaxation of skeletal muscle:

- **Potent and long acting**
- **In ordinary dosage, does not reduce normal muscle strength or reflex activity**
- **Beneficial in 94.4% of tested cases of acute back pain due to muscle spasm**
- **Relatively free from adverse side effects**

Supplied: ROBAXIN Tablets (white, scored), 0.5 Gm., bottles of 50 and 500.

Additional information available on request.

A. H. ROBINS CO., INC., Richmond 20, Va. • *Ethical Pharmaceuticals of Merit since 1878*

in peptic ulcer

Results with "... antacid therapy with DAA are essentially the same as ... with potent anticholinergic drugs."

Alglyn®

Dihydroxy aluminum aminoacetate, N.N.R.

In recent years, a number of new synthetic anticholinergic drugs with numerous and varying side effects have been investigated for treatment of peptic ulcer. However, a double-blind study conducted recently by Cayer et al suggests that the use of such anticholinergic drugs is seldom necessary. The authors concluded that "The percentage of 'good to excellent' results obtained in patients on continuous long-term antacid therapy with DAA (74%) is essentially the same as that previously noted in ulcer patients treated under similar conditions with potent anticholinergic drugs alone."

The authors' choice of dihydroxy aluminum aminoacetate (DAA) was based on the fact that "the tablet form of DAA (is) more active than a variety of straight aluminum hydroxide magmas." They further commented that "Because of the convenience of tablet medication as compared with the liquid gel—a convenience which in the use of other tablets is gained at the expense of therapeutic effectiveness—dihydroxy aluminum aminoacetate was used exclusively."

ALGLYN (dihydroxy aluminum aminoacetate) Tablets are supplied in bottles of 100 tablets (0.5 Gm. per tablet).

BRAYTEN PHARMACEUTICAL COMPANY • *Chattanooga 9, Tennessee*

there's pain and inflammation here... it could be mild or severe, acute or chronic, primary or secondary fibrositis—or even early rheumatoid arthritis

more potent and comprehensive treatment than salicylate alone

. . . assured anti-inflammatory effect of low-dosage corticosteroid[1]

. . . additive antirheumatic action of corticosteroid plus salicylate[2-5] brings rapid pain relief; aids restoration of function.

. . . wide range of application including the entire fibrositis syndrome as well as early or mild rheumatoid arthritis

more manageable corticosteroid dosage

. . . much less likelihood of treatment-interrupting side effects[1-6]

. . . simple, flexible dosage schedule

in any case
it calls for

Sigmagen®

corticoid-salicylate compound

tablets

Composition

METICORTEN® (prednisone)	0.75 mg.
Acetylsalicylic acid	325 mg.
Aluminum hydroxide	75 mg.
Ascorbic acid	20 mg.

Packaging: SIGMAGEN Tablets, bottles of 100 and 1000.

References: 1. Spies, T. D., et al.: J.A.M.A. 159:645, 1955. 2. Spies, T. D., et al.: Postgrad. Med. 17:1, 1955. 3. Gelli, G., and Della Santa, L.: Minerva Pediat. 7:1456, 1955. 4. Guerra, F.: Fed. Proc. 12:326, 1953. 5. Busse, E. A.: Clin. Med. 2:1105, 1955. 6. Sticker, R. B.: Panel Discussion, Ohio State M. J. 52:1037, 1956.

Acute conditions: Two or three tablets four times daily. After desired response is obtained, gradually reduce daily dosage and then discontinue.

Subacute or chronic conditions: Initially as above. When satisfactory control is obtained, gradually reduce the daily dosage to minimum effective maintenance level. For best results administer after meals and at bedtime.

Precautions: Because SIGMAGEN contains prednisone, the same precautions and contraindications observed with this steroid apply also to the use of SIGMAGEN.

SCHERING CORPORATION • BLOOMFIELD, N. J.

SG-J-64B

Schering

YOU CAN SEE THEM RESPOND TO "TOTAL EFFECT" NUTRITIONAL SUPPORT

GEVRAL-T

HIGH POTENCY VITAMIN AND MINERAL SUPPLEMENT LEDERLE

CAPSULES

For a really rapid response in debilitated patients, prescribe new GEVRAL T, the unique *"total effect"* nutritional supplement. Actually *six nutritive formulas in one*, each high potency GEVRAL T Capsule includes:

A COMPLETE, HEMATINIC SUPPLEMENT . . . including non-inhibitory intrinsic factor for enhanced B_{12} absorption, plus Folic Acid, Vitamin C, and Iron.

ALL THE FAT-SOLUBLE VITAMINS...including Vitamin K . . . in ample amounts.

A COMPLETE B-COMPLEX COMPONENT . . . in high dosage quantities.

AMINO ACID SUPPLEMENT, l-Lysine . . . for fuller utilization of ingested protein.

LIPOTROPIC FACTORS, CHOLINE AND INOSITOL

12 IMPORTANT MINERALS AND TRACE ELEMENTS

Your patients get even more nutritional support for their money with economical GEVRAL T . . . *supplied in an attractive, on-the-table jar.*

Each capsule contains:

Vitamin A	25,000 U.S.P. Units
Vitamin D	1,000 U.S.P. Units
Vitamin B_{12}	5 mcgm.
Thiamine Mononitrate (B_1)	10 mg.
Riboflavin (B_2)	10 mg.
Pyridoxine HCl (B_6)	2 mg.
Vitamin E (as tocopheryl acetate)	5 I. U.
Vitamin K (Menadione)	2 mg.
Ascorbic Acid (C)	150 mg.
Calcium Pantothenate	5 mg.
Niacinamide	100 mg.
Folic Acid	1 mg.
Calcium (as $CaHPO_4$)	107 mg.
Phosphorus (as $CaHPO_4$)	82 mg.
Iron (as $FeSO_4$)	15 mg.
Magnesium (as MgO)	6 mg.
Potassium (as K_2CO_4)	5 mg.
Iodine (as KI)	0.15 mg.
Boron as $Na_2B_4O_7 \cdot 10H_2O$)	0.1 mg.
Copper (as CuO)	1 mg.
Manganese (as MnO_2)	1 mg.
Fluorine (as CaF_2)	0.1 mg.
Zinc (as ZnO)	1.5 mg.
Molybdenum (as $Na_2MoO_4 \cdot 2H_2O$)	0.2 mg.
Choline Bitartrate	25 mg.
Inositol	25 mg.
l-Lysine Monohydrochloride	25 mg.
Rutin	25 mg.
Purified Intrinsic Factor Concentrate	0.5 mg.

DOSAGE: 1 capsule daily for the treatment of vitamin and mineral deficiencies, or more as indicated.

SUPPLIED: Bottles of 100 capsules.

LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK Lederle

℞ trichotine (FESLER)

superior vulvovaginal therapy

with

trichotine®

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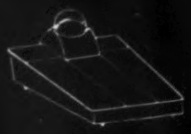

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1. Sc. Exhibit, A.M.A. Meeting, Dec. 2-6, 1957.
2. Sc. Exhibit, Mich. State Med. Meeting, Sept. 25-27, 1957.
3. Gadek, R. J.: Report 912:1957.
4. Sc. Exhibit, N. Y. State Med. Meeting, Feb. 18-21, 1957.

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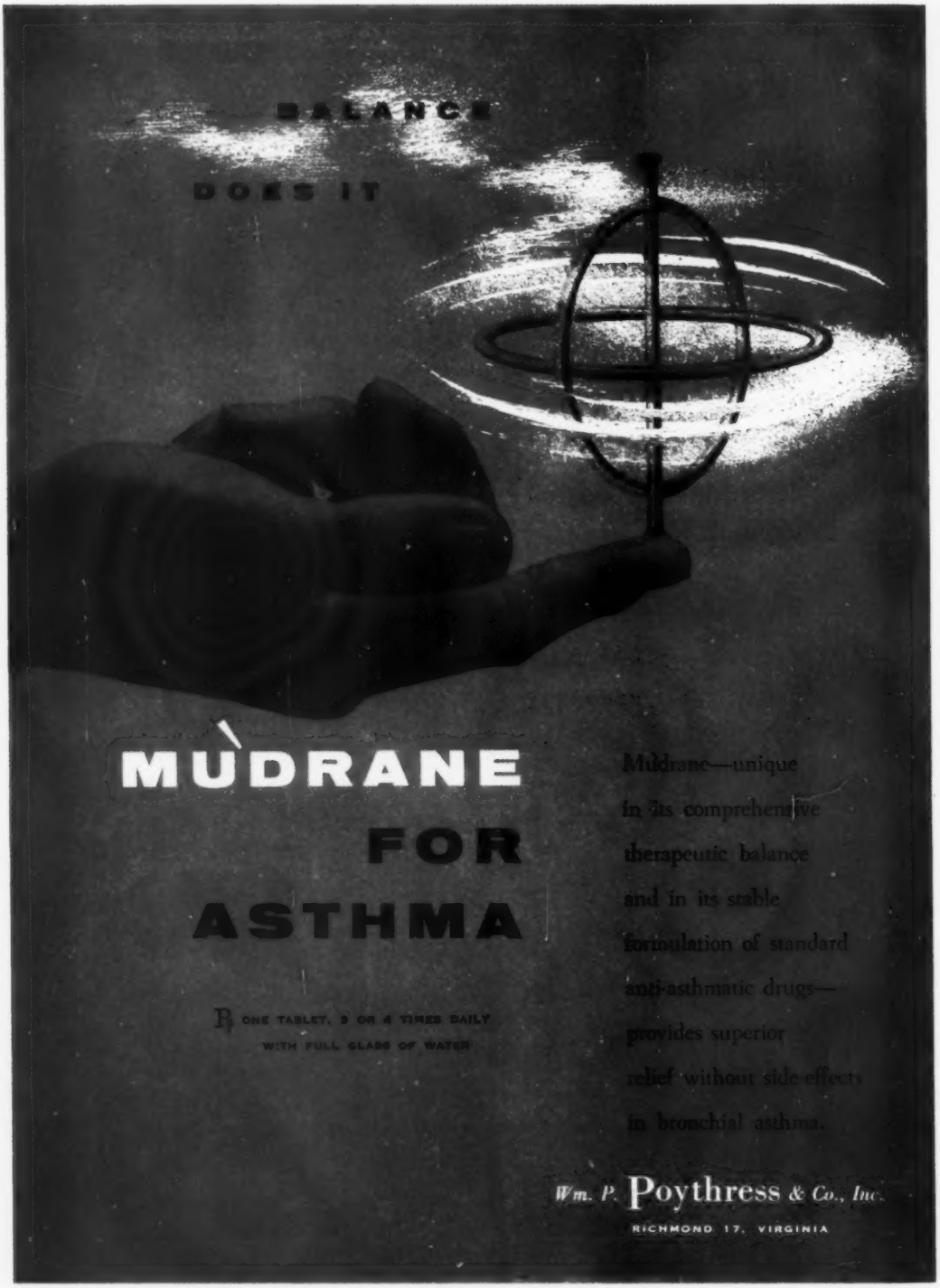
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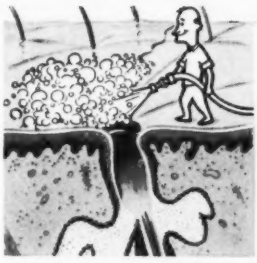

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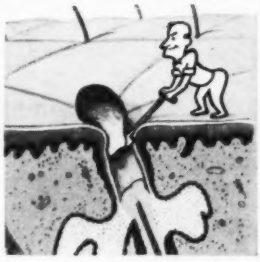

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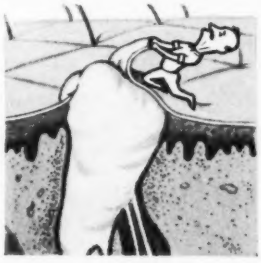

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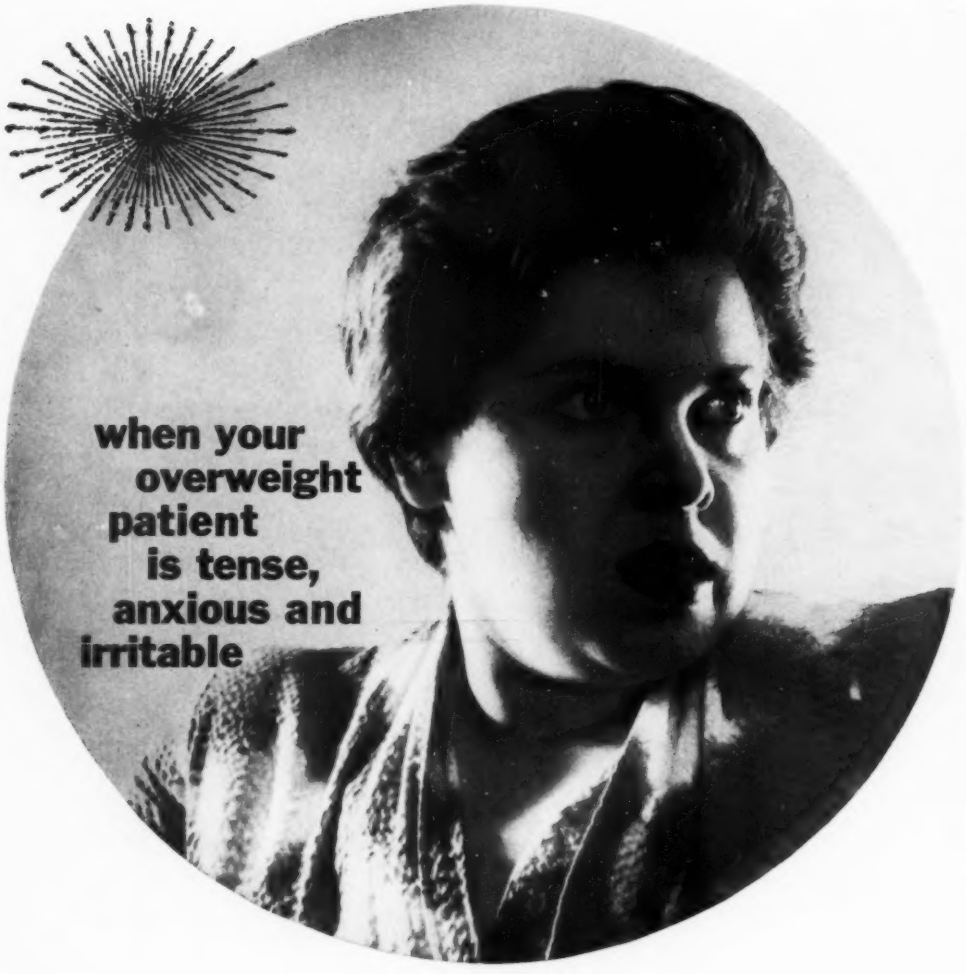

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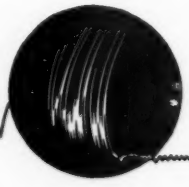
1. Jones, Georgeanna S. and Smith, Frank: Am. J. Obstet. Gynecol., Vol. 67: No. 3, 628-633, 1954.
2. Majewski, J. T. and Jennings, T.: Obstetrics & Gynecology, Vol. 5, No. 5, 1955.
3. Majewski, J. T. and Jennings, T.: Obstetrics & Gynecology, Vol. 9, No. 3, 1957.



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Southern Medical Journal

PUBLISHED BY SOUTHERN MEDICAL ASSOCIATION

March 1958

The Heart in Rheumatoid Arthritis*

HOWARD L. HOLLEY, M.D., *Birmingham, Ala.*

The cardiac lesions found in patients having rheumatoid arthritis have always been intriguing from the viewpoint of etiology and pathogenesis. The author considers this problem.

THE SYSTEMIC NATURE OF RHEUMATOID ARTHRITIS has only been recently appreciated. It was formerly believed that the lesions of this disease were confined principally to the joint structures and other parts of the musculoskeletal system while the visceral organs were rarely if ever involved. However, it was noted early that a higher incidence of cardiac lesions could be demonstrated at necropsy in patients with rheumatoid arthritis than in the population at large. During the past several years a fairly extensive literature concerning these heart changes has appeared. Originally the lesions were thought to be the result of an earlier bout of rheumatic fever because it was the considered opinion that the incidence of rheumatic heart disease in patients with rheumatoid arthritis was significantly higher than in the general population. This finding gave impetus to the belief, first suggested by Klinge,[1] that rheumatic fever and rheumatoid arthritis are different manifestations of the same disease, the basic pathophysiology being the same.

Pericarditis has long been recognized as a common finding at autopsy in patients with rheumatoid arthritis. In one report of necropsy findings in 66 cases of rheumatoid arthritis, 50 per cent had evidence of pericarditis.[2] Clark and Bauer,[3] writing in 1948, stated that in 445 cases of this disease coming to autopsy, 44 per cent had evidence of pericarditis. A granulomatous pericarditis was observed in Bauer's[3] series and was also described later by Bevans and collaborators.[4] The pathologic picture of these granulomatous lesions was strikingly similar to those seen in the subcutaneous nodules characteristic of rheumatoid arthritis. Though the granulomatous type pericarditis has been observed in rare instances of rheumatoid arthritis, the fibrinous type is much more common. However, it is difficult to determine what proportions of the healed cases were originally granulomatous or fibrinous in nature.

The pericarditis of rheumatoid arthritis is not usually recognized clinically, although EKG changes and pericardial friction rubs have been observed. In juvenile rheumatoid arthritis, however, pericarditis is not only more frequently found at autopsy (it was present in the three original cases described by Still[5]) but is also more commonly recognized during life.

The relatively high incidence of valvular lesions found at necropsy in patients having rheumatoid arthritis has been mentioned by numerous investigators. Baggenstoss and Rosenberg[6] found 14 of 25 cases with cardiac lesions which they considered indistinguishable from those of rheumatic fever. Later, in an extension of their original series, 16 of 30 cases were classified as having rheumatic heart lesions, and two additional cases were considered doubtful but probably of the same origin.[7] Their studies failed to identify, however, the criteria they employed for designating a lesion to be of rheumatic fever origin. There was clinical evidence of rheumatic fever in only two of their patients. Graef, Hickey and Altman[2] reviewed the necropsy findings in 66 cases of rheumatoid arthritis and found 19 with mild valvular deformity, one with mitral stenosis, and 5 with old rheumatic valvulitis. However, no attempt was made to correlate these necropsy

*Chairman's Address, read before the Section on Medicine, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

findings with a clinical history of rheumatic fever.

Although the literature has remained controversial, it may be said in general that most clinical studies have failed to confirm the earlier observations of a high incidence of rheumatic heart disease in patients with rheumatoid arthritis, while pathologic investigations have indicated that the two diseases may co-exist frequently. There is now, however, clinical evidence that valvulitis and other stigmata of rheumatic heart disease are, in fact, infrequent in patients with rheumatoid arthritis, except when a straightforward clinical history of rheumatic fever can be obtained.

It is now believed that in the absence of definitive diagnostic criteria, pathologists have in general employed criteria for the diagnosis of rheumatic heart disease that are far from specific. Although few individuals would doubt that the finding of Aschoff bodies is always the consequence of rheumatic carditis, the significance of minor sclerotic and inflammatory changes in the heart is highly debatable.

The absence of a history of acute attacks of rheumatic fever in these autopsy reports is noteworthy. Furthermore, clinical signs of rheumatic heart disease were absent in the majority of patients subsequently found to have valvular deformities at autopsy. It seems entirely probable that the postmortem incidence of valvulitis reported in rheumatoid arthritis represents the healed stage of endocardial lesions similar to those seen in other serosal surfaces of the body in this disease.

Aortic valvular disease, particularly with aortic insufficiency, is apparently not an uncommon finding in rheumatoid spondylitis.[8-10] The heart disease in this variant characteristically follows an episode of acute polyarthritis; it is more common in patients in whom chronic peripheral rheumatoid arthritis develops in spondylitis, and in which uveitis or iritis accompanies the disease.

Since rheumatoid spondylitis itself is relatively uncommon, not many cases with associated heart disease have been reported or are available for study. Schilder, Harvey, and Hufnagel's[9] series of aortic insufficiency showed 5 per cent associated with rheumatoid spondylitis in their first 100 cases of lesions of aortic valvular disease evaluated for surgical repair. Their patients had striking similarities in many respects. All had severe rheumatoid spondylitis with a "poker spine" deformity. The average duration of the disease was 23 years. The average age when first seen was 49 years, and the duration of known heart disease ranged from 2 to 10 years, with an average of 7 years. Pathologic study of the hearts in 3 of these patients showed involvement only of the aortic valve. No Aschoff bodies were seen in several sections, and there was extensive pathologic destruction of all three layers of the root of the aorta. The mitral valves were not involved.

Clark and Bauer[3] had observed as early as 1948 three cases in their extensive autopsy series that showed an unidentified aortitis in which there was an aortic valvulitis that resembled the typical pannus formation seen in synovial cavities. Recently, Clark, Kulka, and Bauer[10] have reviewed a series of 22 patients who presented symptoms of rheumatoid aortitis and aortic valvular incompetence that they had observed over a period of 20 years, beginning with two cases in which the autopsies were performed in 1936. Originally these autopsies were described by Mallory[11] who erroneously thought the findings in the aorta and aortic valve to be a result of syphilitic infection, although collateral evidence did not support this assumption. All of their patients were males, whose ages ranged between 18 and 64 years and, with two exceptions, all had some degree of spondylitis. The metacarpophalangeal or interphalangeal joints were involved in about half of the patients. Fifty-nine per cent of their patients had uveitis; subcutaneous nodules were not observed. Eighteen per cent had psoriasis. These authors call attention to the relative absence of previous reports of this lesion in the literature; an early report had been made of a patient who had juvenile rheumatoid arthritis.[12]

Histologically the cardiac lesions were significant in their striking similarity to those of syphilitic aortitis with aortic regurgitation. The aortic ring was dilated, with distortion of the cusps which showed varying degrees of fibrosis with thickening, retraction, and rolling of the free margins. Focal calcareous deposits were present in two lesions of more than nine years duration. The mitral valve

was not involved. Aortitis was present and it was characterized grossly by discrete intimal plaques which seemed to be continuous with the valvular lesions. The plaques appeared to be of different stages of development and varied from a "pannus-like" layer to those that were thickened and calcified. The coronary ostia were involved in some instances.[10]

This clinicopathologic entity has received little attention in the past, no doubt due to its similarity to syphilitic aortitis, for which it is easily mistaken. The course of the heart disease is not unlike that seen with aortic insufficiency of syphilitic or rheumatic heart disease; i.e., marked left ventricular hypertrophy, involvement of the coronary ostia, congestive heart failure and death.

That this process is not due to rheumatic fever is based on the presence of unequivocal evidence of concurrent rheumatoid arthritis and, especially, with an absence of a clinical history of rheumatic fever together with the uniform absence of Aschoff bodies, perivascular "onion skin" scars and other rheumatic stigmata in the pathologic material. The occurrence of a diastolic aortic murmur in patients with rheumatoid spondylitis, especially during an exacerbation of the arthritis and particularly in the presence of uveitis, is considered of diagnostic significance. The spondylitis occasionally may not be a prominent finding and can be demonstrated only by roentgenologic examination. Contrary to the earlier reports, the heart disease associated with rheumatoid spondylitis, is not always benign. Most often the clinical course of the disease is similar to that of aortic insufficiency due to other causes, death being due to intractable heart failure. Sudden death has been reported.

We have now observed 7 patients with aortic insufficiency associated with rheumatoid arthritis. These have been seen by the Rheumatic Disease Consultation Service at the University Hospital, Hillman Clinic and the Veterans Hospital in Birmingham. These patients do not by any means represent a cross section of the rheumatoid population in this area, therefore, it would be impossible to estimate adequately the incidence. Obviously, only the patients with relatively severe lesions of the disease are admitted to the hospital, clinic and consultation service; the milder cases are treated by private physicians. Clark and collaborators,[10] estimate this lesion occurred in 2 per cent of patients with a diagnosis of rheumatoid arthritis but it would be reasonable to assume that it occurs much more frequently in males with rheumatoid spondylitis.

Our group of patients is interesting in that it appears strikingly similar to the group reported by Clark and co-workers.[10] Five of the patients had uveitis, 6 had rheumatoid spondylitis (one had no clinical or roentgenologic evidence of spinal involvement), all had peripheral joint involvement and one had the classical symmetrical ulnar deviation of the hands. All the patients had unequivocal findings of aortic insufficiency. The ages ranged from 28 to 47 years, and the duration of the disease was from 3 to 12 years, with an average of 9 years. It was difficult to determine from the history, except in one patient, the time of the onset of the valvular lesions; most were present on our initial examination (Table 1).

The course of one of these individuals has been followed from the onset of the illness. His disease was characterized by an episodic course with skin lesions, fever, polyarthritis, and severe uveitis. At no time was there a history consistent with spinal involvement although the x-ray examination revealed classi-

TABLE 1

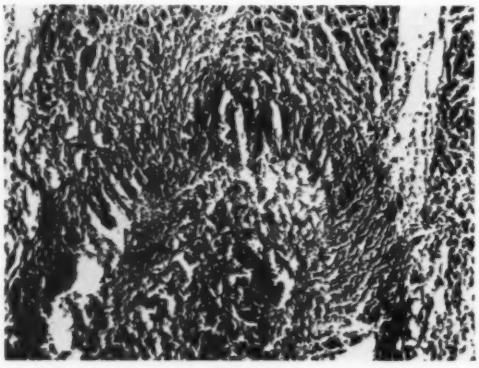
AORTIC INSUFFICIENCY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Case No.	Sex-Race	Age	Duration of Disease	Manifestations of Arthritis: Periph-eral	Spine	Uveitis	Skin	Subcut. nod.	Cardiovascular Findings: Aortic insuff.	Mitral	Peri-carditis	Serological Agglutination: SSA	Latex	STS
1.	CM	37	12 yrs.	x	0	?	0	0	x	0	0	0	0	0
2.	WM	47	10 yrs.	0	x	x	0	0	x	0	0	—	—	0
3.	WM	38	7 yrs.	x	x	x	0	0	x	0	0	0	0	0
4.	WM	28	3 yrs.	x	x	0	0	0	x	0	?	0	0	0
5.	CM	35	11 yrs.	x	x	x	x	0	x	0	0	0	0	0
6.	WM	54	7.5 yrs.	x	x	x	x	0	x	?	0	0	0	0
7.	CM	31	12 yrs.	0	x	x	0	0	x	0	0	0	0	0

cal bilateral changes in the sacro-iliac joints. The cardiac involvement was noted 4 years after the onset of illness. Although the basilar murmur is variable in character, it has at times been high pitched and has been described as a "cooing dove" type murmur, occupying the entire diastole. An Austin-Flint murmur is also considered to be present. He has had one severe bout of congestive heart failure, and is now being maintained on digitalis and a low-salt diet. For the most part, however, the heart lesions in this series of patients have appeared to be relatively mild; some have now been observed for more than a year.

The other type of heart lesion described in rheumatoid arthritis is the granulomatous lesion involving the pericardium, valvular leaflets and myocardium, which is histologically indistinguishable from the subcutaneous necrobiotic nodule. These localized areas are granulomatous in nature and appear in histologic section as deeply eosinophilic staining acellular amorphous material, so-called fibrinoid necrosis (Fig. 1). This process is observed frequently to invade the valve ring and leaflets together with the surrounding myocardium. There occurs fibroblastic proliferation at the periphery of the area of degeneration together with round cell infiltration in the characteristic pattern seen in subcutaneous rheumatoid nodules. Giant cells may be observed in the periphery of the lesion.[13] The endocardium may appear intact but the valve may be thickened and on healing, contraction and stenosis develop.

FIG. 1



Granulomatous nodule in the myocardium with characteristic surrounding radiating connective tissue proliferation.

Bevans and associates[4] described two cases of rheumatoid arthritis which they believed represented a malignant form of the disease. Both patients were females who showed evidence of pericarditis and endocardial granulomatous lesions at autopsy. The nodules in the pericardium were characterized by different stages of development and regression. The cellular structure of these nodules were not unlike those of the subcutaneous nodules of rheumatoid arthritis and involved also the aortic, mitral and tricuspid valves. There were no Aschoff bodies. In one instance the lesion invaded the chordae tendineae of the left ventricle. It is interesting that the normal gross appearance of the valves often belied alterations in their histologic structure.

The process differs, then, from the carditis of rheumatic fever in the granulomatous character of the valvular lesions, in the lack of Aschoff bodies and also in the concomitant finding of the granulomatous lesions elsewhere in synovial and serous membranes of the viscera.

In the autopsy series reported by Graef, Hickey and Altman,[2] there were two patients who showed a similar lesion in the heart. Likewise, in 1948, Raven and associates[13] and Gruenwald[14] also reported patients with peripheral rheumatoid arthritis who showed granulomatous areas in the myocardium at necropsy which they termed necrobiotic nodules. Bauer and Clark,[15] writing in 1948, stated that in their extensive autopsy series of rheumatoid arthritis, they had observed two individuals whose hearts showed pericardial and endocardial nodules indistinguishable from the subcutaneous nodules of rheumatoid arthritis. Gruenwald[14] has reported a case of peripheral rheumatoid arthritis with granulomatous nodules in the right atrium and in the tricuspid valve. The cardiac involvement was not the primary cause of death in these patients in contradistinction to the effect of the aortic lesions in spondylitis.

It should be remembered that Bennett, Zeller and Bauer,[16] reporting in 1948, found many similarities, but also important differences, and concluded that the nodules of rheumatoid arthritis and rheumatic fever differ as much one from another as do the granuloma of tuberculosis and syphilis.

We have recently had the opportunity to observe a patient with peripheral rheumatoid arthritis and subcutaneous nodules, marked muscle atrophy and contractures. The disease had been present for 13 years. At autopsy granulomatous nodules were found in the heart and other viscera, identical with those found in the peripheral subcutaneous tissue of the extremities. The pericardium, endocardium, and myocardium were involved. Although there were no serologic tests for rheumatoid arthritis performed on this patient, one could postulate that the probability is that the sensitized sheep cell agglutination test would have been positive. A remarkable correlation has been noted between the occurrence of peripheral subcutaneous nodules and a positive serologic reaction.[17] Cultures taken from the heart at autopsy failed to show any growth.

Similarly, we have had the opportunity of reviewing the autopsy findings on a white male patient who had been suffering with rheumatoid arthritis for 12 years, finally becoming an invalid during the last several years of his life. He had had prolonged cortisone therapy. Tissue sections of the viscera revealed rheumatoid granulomatous nodules in the myocardium, epicardium and diaphragm. There were healed rheumatoid nodules in the subcutaneous tissue of the forearm. Again, attempts to culture pyogenic organisms and fungi were of no avail.

Sokoloff[18] has observed another type of cardiac involvement that constitutes an interstitial myocarditis in patients with peripheral rheumatoid arthritis. The histologic appearance, however, lacks specificity and simulates lesions seen in other types of disease, namely, drug hypersensitivity, trichinosis, viral and Fielder's myocarditis. A coronary arteritis has been observed in autopsy material from patients with rheumatoid arthritis.[19] These arterial changes are not unlike the generalized vascular lesions found in the other viscera of this disease.

The several patterns of involvement, i.e., the leaflets, myocardium and pericardium and arteritis, often co-exist in the same specimen and constitute the picture of a pancarditis. The varied histologic patterns may result from the differences in the relative intensity, as well as the duration of the process with its sequelae of proliferations and reparative elements. Concomitantly similar focal lesions may be seen in other viscera of the body.

The possibility of cortisone and other similar steroids producing these lesions has been suggested but the fact that well substantiated reports of their occurrence prior to the introduction of this type of therapy would seem to preclude this fact.[20] There is a definite possibility, however, that these drugs may possess a potentiating effect and the incidence of visceral involvement may be increasing. The considerably higher incidence of rheumatoid heart disease reported pathologically by Levin and co-workers[21] than that of other investigators would be in accord with this hypothesis.

It would be reasonable to assume that the lesions in the aortic valve and the root of the aorta of rheumatoid spondylitis represent healed granulomatous lesions similar to those found in the valvular leaflets, pericardium, and myocardium. However, there is little or no evidence to support the fact that these lesions originated in this manner, although some of the scarring of the intima and adjacent myocardium may be of this origin. Without entering into the controversy as to whether peripheral rheumatoid arthritis and spondylitis are one and the same disease process, it can be said that there are features that indicate that these two cardiac lesions may be distinct histologic entities. The aortic lesions have been observed mostly in patients (but not all of them) with unequivocal evidence of spondylitis. The relatively few patients of this group who have been studied with the serologic tests for rheumatoid arthritis, i.e., the sheep cell agglutination test and the latex modifications, have had a negative reaction, while those having the granulomatous lesions, as reported by Bevans and co-workers,[4] had positive agglutination tests for group A streptococci. These patients all had peripheral rheumatoid arthritis; some had clinical evidence of subcutaneous nodules. There was no involvement of the spine.

The fact that the aortic lesions are found predominantly in the male probably reflects the higher incidence of rheumatoid spondylitis in that sex. Likewise, subcutaneous nodules, which are histologically indistinguishable from the granulomatous lesions found in the heart, are not characteristically seen

in the rheumatoid spondylitis. There appears to be a distinctive predilection for the aortic valve and adjacent ascending aorta with scarring of the intima in rheumatoid spondylitis, with little or no evidence of involvement of other valvular areas in contradistinction to the granulomatous lesions which involve the mitral and tricuspid as well as the aortic valves. Likewise, the infiltration of the cardiac musculature with the granulomatous lesions has not been described in patients with spondylitis.

Summary and Conclusions

The occurrence of cardiac lesions in patients with rheumatoid arthritis has been described. The literature pertinent to these changes has been reviewed. The evidence that the heart lesions seen in rheumatoid spondylitis and those in classical peripheral arthritis may be distinct entities has been presented. The possibility that the increasing use of adrenal steroids may have resulted in an increased incidence of visceral lesions in individuals suffering with rheumatoid arthritis has been postulated, however, it cannot be overlooked that the increasing awareness of the occurrence of these changes has resulted in their more frequent recognition.

Acknowledgment

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Chlorpromazine Jaundice: The Effect of Continued Chlorpromazine Ingestion in the Presence of Chlorpromazine Jaundice*

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This paper makes some most pertinent observations on the jaundice and liver biopsies in patients suffering from chlorpromazine jaundice.

THE MODERN PHYSICIAN is in a very fortunate position. The "soma" pill of fiction has become a readily available antidote for today's reality. Through it the sad patient may be made happy, and the happy patient appropriately sad, and, under the proper circumstances, not a few of these patients may also be made jaundiced.

It is to the problem of this jaundice, most notably associated with chlorpromazine, that this paper is addressed.

Jaundice has been thought to occur in approximately 1 per cent of all patients receiving chlorpromazine.[1,2] The general character of this jaundice is that of an intrahepatic obstructive lesion.

The etiology of chlorpromazine jaundice is obscure and its treatment empirical. The only general agreement on the problem rests in the concept that when jaundice appears the etiologic agent must be discontinued.

The present report is based on a study of 4 patients in whom the administration of chlorpromazine was continued without change following the appearance of jaundice.

Methods and Materials

Four patients, 3 female, 1 male, all inmates of a state mental hospital and ranging in age from 49 to 79 years, were studied following the appearance of jaundice. Early studies in 2 of these patients (subjects 1 and 2) were incorporated in a previous report.[3] All of the patients had been receiving chlorpromazine in dosages of 150 to 200 mg. per day for from 25 to 39 days prior to the appearance of jaundice (Table 1). In each instance, chlorpromazine was continued without change in dosage until all clinical and laboratory evidence of jaundice had disappeared.

All 4 patients were studied in a manner similar to that previously reported.[3] Liver function tests done are indicated in tables 1 and 2.

In 3 of the 4 subjects, initial laboratory studies and liver biopsies were obtained within 3 to 5 days of the appearance of clinical jaundice. In patient 2 there was a 12 day interval between the onset of icterus and the initial laboratory study. A liver biopsy attempt on this patient was unsuccessful.

A second series of liver function tests was obtained on all patients 10 to 21 days following the initial observations.

A third battery of hepatic function tests, together with liver biopsies in all subjects, except patient 2, was performed 42 to 68 days later and was the final study on subjects 2, 3, and 4. Patient 1 had one additional liver function battery done 151 days following onset of jaundice.

Results

The results and findings of this study are recorded in tables 1 and 2 and figures 1, 2, and 3. The total protein remained within normal limits throughout the period of study in all subjects. However, the serum albumin was low in all subjects initially, and in patient

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TABLE 1

Patient	Age	Sex	CPZ Dose Mg./d	CPZ R_X Start	Jaundice Start	CPZ Stop	Date of Study	Total Protein (6-7.5)	Albumin (4-5)	Cephalin Flocculation (0-1/24)	Thymol Turbidity (0-4)	Serum Alkaline Phosphatase BU (0.5-4)	Total Serum Bilirubin (0.8-1.2)	Direct Serum Bilirubin (0.6-0.25)	Total Cholesterol (150-250)	% Cholesterol Ester (60-80)	Lipid Phosphorous (8-12)	
							Oct. 7	6.5	3.2	Neg.	1.6	58	8.8	1.4	273	43	22	Liver Biopsy
1	79	F	150	Aug. 26	Oct. 4	Nov. 25	Oct. 28	6.	3.4	Neg.	1	40	0.8	0	244	70	13.3	
							Dec. 9	6.1	3.3	Neg.	1	7.6	0.4	0	196	80	12.4	Liver Biopsy
							Mar. 7	5.8	3.3	Neg.	1	4.9	0.1	0	162	63	10.4	
							Oct. 7	6.6	3.6	Neg.	2	28	3.6	1.4	295	62	17	No Biopsy
2	71	F	150	Aug. 26	Sept. 26	Cont.	Oct. 28	6.7	4.2	Neg.	2	10.3	0.7	0	274	74	12.5	
							Dec. 9	6.1	3.4	1—	1	3.7	0.5	0	216	76	11.5	
							Dec. 9	6.7	3.9	Neg.	1.5	7	1.9	0.5	216	74	12.4	Liver Biopsy
3	49	F	200	Nov. 11	Dec. 6	Cont.	Dec. 19	6.1	3.4	Neg.	1.5	4.6	0.9	0.3	165	81	9	
							Mar. 7	6.5	4.0	Neg.	2	2.5	0.2	0.1	194	74	9.4	Liver Biopsy
							Dec. 19	6.1	3.8	Neg.	1	10.3	5.8	1.8	222	73	10.3	Liver Biopsy
4	55	M	200	Nov. 10	Dec. 14	Cont.	Dec. 29	—	—	——	——	12.6	3.35	3.15	—	—	—	
							Mar. 7	6.3	4.2	1—	1	1.7	0.6	0.1	187	73	9.9	Liver Biopsy

TABLE 2

Patient	Date of Study	Albumin (50-55)	α 1 Glob. (3-4)	α 2 Glob. (8-9)	B Glob. (12-15)	Gamma Glob. (16-20)
	Oct. 7	43.3	4.3	12.1	17.3	22.9
1	Oct. 28	44.7	4.3	12.8	20.9	17.4
	Dec. 7	41.6	4.2	18.5	15.4	20.3
	Oct. 7	47.2	4.5	8.5	12.5	27.3
2	Oct. 28	45.7	3.6	13.1	16.7	20.8
	Dec. 9	54	4.5	16.4	13.4	17.7
	Dec. 9	50.2	3.6	9.8	22.2	14.2
3	Dec. 19	50.8	3.6	18.2	17.5	12.9
	Mar. 7	61.3	2.4	6.3	11.1	19.0
4	Dec. 19	52.3	5.0	7.8	15.6	19.3
	Mar. 7	59.4	3.7	8.0	10.2	18.7

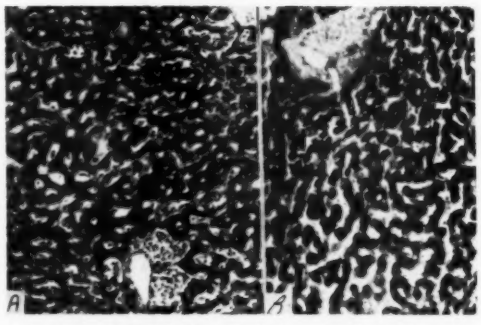
l never did attain normal levels during the study. In view of similar findings previously reported on a group of nonicteric patients in the same institution,[3] it is felt that the nutritional status of the patients was the important influencing factor in the serum albumin levels.

In table 2 are recorded the changes in all protein compartments as measured by serum electrophoresis. No consistent pattern can be found in relation to the appearance or clearing of jaundice.

The cephalin flocculation and thymol turbidity determinations were normal throughout the study in all subjects.

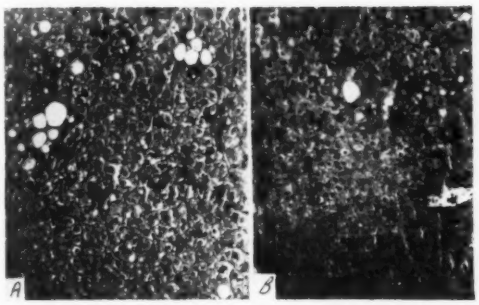
The serum alkaline phosphatase was elevated initially in every patient, ranging from 7 to 58 Bodansky units. The return to normal was much more gradual than the total serum bilirubin levels which were also elevated (1.9 to 8.8 mg./100 cc.) in all subjects at the start of the study.

FIG. 1



(A) Liver biopsy (Subject 1) during jaundice. PAS stain (X 100). Note periportal infiltration, bile canalicular plugging and reduction of glycogen in some liver cells. (B) Liver biopsy (Subject 1) after jaundice. PAS stain (X 100). Note even glycogen distribution.

FIG. 2



(A) Liver biopsy (Subject 3) during jaundice. H & E stain (X 100). Note vacuolar fatty change. (B) Liver biopsy (Subject 3) after jaundice. H & E stain (X 100). Fatty infiltration persists.

In patient 1, a slight elevation of the serum alkaline phosphatase (4.9 Bodansky units) persisted 130 days after all evidence of jaundice had cleared.

The total serum bilirubin returned to normal in from 10 to 21 days in three of the patients. In patient 4, however, a normal bilirubin level is not recorded until 68 days after original study. In this subject, clinical jaundice cleared much earlier but no laboratory studies were done until that date.

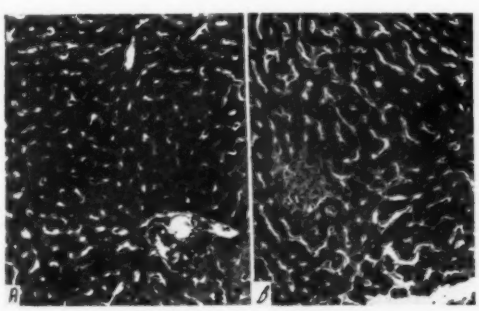
The direct bilirubin was elevated in all subjects at the time of original observation, ranging from (0.5 to 1.8 mg. per 100 cc.). Only in patient 4 was there significant elevation at the time of the second study 10 to 21 days later.

In two subjects, 1 and 2, the total cholesterol levels were high initially, 273 and 295 mg. per 100 cc. respectively, but returned to normal during the study. In patient 1, the percentage of cholesterol esters was low (43 per cent) at the time jaundice occurred but not thereafter.

The serum lipid phosphorous tended to be higher at the time of onset of jaundice than at any other time in the course of the study. In patients 1, 2, and 3, the levels were definitely abnormal initially.

Liver biopsies were obtained from all subjects except patient 2, in whom biopsy attempts were unsuccessful (Figs. 1, 2, and 3). In subjects 1 and 4 (Figs. 1, A and 3, A) the initial biopsies showed plugging of the bile canaliculi, retention of bile in hepatic cells, and slight to moderate periportal infiltration. In subject 3 (Fig. 2, A), only vacuolar fatty change was noted. Subsequent biopsies obtained on all three subjects following the clearing of jaundice were normal except for persistence of some fatty vacuolar change in subject 3 (Figs. 1, B, 2, B and 3, B).

FIG. 3



(A) Liver biopsy (Subject 4) during jaundice. H & E stain (X 100). Note periportal infiltration and scattered bile plugs. (B) Liver biopsy (Subject 4) after jaundice. H & E stain (X 100). Essentially normal liver.

Discussion

As previously reported, 8 nonjaundiced subjects who received massive doses of chlorpromazine (1,500 to 3,500 mg. per day) for six months demonstrated no changes in liver function or morphology. This same report contained a review of 48 cases of chlorpromazine jaundice found in the literature and indicated that the average duration of jaundice was 41 days.[3] In the present paper, it was noted that the abnormalities in liver function and morphology associated with the appearance of jaundice were of relatively brief duration, ranging from 10 to 68 days, despite continuation of chlorpromazine. Consequently, it is felt that the concept of chlorpromazine being a "hepatotoxic agent capable of causing severe liver damage"[4] is not correct. Every finding in the present study supports the view of Issacs and associates,[1] that the jaundice is not due to a direct toxic action of chlorpromazine on the liver.

Kelsey and his co-workers[5] and others[1,6] have suggested that chlorpromazine jaundice occurs more frequently in patients with underlying liver disease than in those with normal livers. Of the 4 patients presently under discussion, only one demonstrated slight fatty changes on liver biopsy and none showed any other changes either during or after the episode of jaundice suggestive of hepatocellular disease.

Gambescia and collaborators[2] believe that the mechanism of jaundice following chlorpromazine ingestion is primarily a hypersensitivity response in which the cholangiole is the end organ. It seems doubtful that a hypersensitivity response was the cause of the jaundice in the present series of patients. Ordinarily a hyperergic response should be either prolonged or intensified by continued exposure to the allergen. And, therapy for a hypersensitivity response is predicated in large part on taking the suspected allergin from the allergic patient.[7] In the present group of patients the continued use of the theoretical allergen (chlorpromazine) did not intensify the existing biochemical or morphologic abnormality, nor did it prolong the period of jaundice in any subject.

Stein and Wright[8] have theorized that chlorpromazine induces some change in the composition of bile that leads to an increase in bile viscosity which could result in its inspissation and resultant jaundice.

In a recent report, Parish and Levine[9] indicated that chlorpromazine induced a significant water diuresis in patients they had studied. This diuresis might well be the source of increased viscosity of the bile suggested by Stein and Wright. However, diuresis and dehydration alone seem insufficient factors to account for the appearance of jaundice.

Menguy and associates[10] have found that in dogs given large doses of chlorpromazine, biliary sphincter spasm occurs and leads to a marked slowing of bile flow. They believe that such a change, if it occurred in the human being, could result in jaundice.

It is possible that a combination of these latter factors is the actual mechanism of chlorpromazine jaundice. However, the present study presents no data to either support or refute this possibility.

The present study is not intended as an endorsement of the practice of continuing chlorpromazine in the face of jaundice. Rather it was designed to clinically test the various concepts regarding the etiology of chlorpromazine jaundice.

As a result of this study, certain conclusions can be drawn:

(a) It is doubtful that chlorpromazine is a specific hepatotoxic agent.

(b) The presence of demonstrable liver disease did not enter into the occurrence of jaundice in any of the present group of subjects.

(c) A hypersensitivity response to chlorpromazine is unlikely in the present group of patients in view of the rapidity with which jaundice cleared despite continued use of the theoretical allergen (chlorpromazine).

(d) A syndrome very similar to the inspissated bile syndrome of children occurs following chlorpromazine. The exact mechanisms involved in this are unknown. It is possible that biliary sphincter spasm and changes in bile composition or viscosity, perhaps related to diuresis and dehydration induced by chlorpromazine, are factors in its occurrence.

(e) This study does indicate that in 4 subjects at least, chlorpromazine could be continued with impunity following the appearance of chlorpromazine jaundice.

Summary and Conclusions

Four patients who developed chlorpromazine jaundice were studied while the drug was continued without change in dosage. Liver function studies were done on at least three occasions throughout the period of observation on all subjects.

Elevations of serum alkaline phosphatase and serum bilirubin levels were noted in all subjects initially. The bilirubin levels tended to return to normal somewhat earlier than did the alkaline phosphatase levels. In all subjects serum lipid phosphorous determinations were higher during jaundice than after recovery.

Liver biopsies were available on 3 of the 4 subjects during and again after clearing of jaundice. Bile canalicular plugging and periportal infiltration were noted in 2 subjects on the first biopsy, but were normal on repeat examination. The third subject showed only some fatty change in both biopsies.

It is clear that in the present group of subjects chlorpromazine was continued with impunity following the appearance of chlorpromazine jaundice. The possibility of chlorpromazine inducing changes in bile viscosity or composition and in biliary sphincter tone was neither supported nor refuted by this study. However, the available data does cast doubt on the likelihood of chlorpromazine

jaundice being due to hepatotoxicity or chlorpromazine sensitivity, or to significant underlying hepatic disease.

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Discussion (Abstract)

Dr. David Cayer, Winston-Salem, N. C. To my knowledge the chlorpromazine jaundice syndrome has not been reproduced in animals. It is of interest that chlorpromazine, in dosage considerably larger than that usually used in human patients, fails to produce abnormalities of liver function, or histologic evidence of toxicity in the livers of small animals such as rabbits and rats.

The study in dogs referred to by the essayist indicated an increase in pressure in the common duct of cholecystectomized dogs. There was considerable increase in the resistance of the biliary sphincter to saline perfusion through the in-lying tube in intact animals. The changes noted are similar to those produced with morphine but of longer duration. It is of interest, in view of the lowered serum proteins noted by Dr. Schneider in his patients, that these changes are intensified in fasting animals. Our findings in jaundiced patients are similar to those described by the author, namely an elevated phosphatase and canalicular plugging. Eosinophilia was not a feature of our own few cases. That chlorpromazine is not primarily hepatotoxic is also indicated by the fact that routine function tests in patients receiving chlorpromazine fail to show significant changes, and patients who have recovered following chlorpromazine jaundice and have died of other causes are usually found to have normal livers at postmortem examination.

I do not feel that the difficulty is due to hypersensitivity nor do I agree with the reasoning of some that improvement following cortisone or ACTH administration necessarily supports such a belief. It has been reported elsewhere that an increased flow of bile of decreased viscosity may follow the administration of steroids.

The occasional development of hepatomegaly and elevated alkaline phosphatase without the occurrence of jaundice would seem to indicate that a considerable amount of bile may be retained within the liver possibly as a result of sphincter spasm. It is conceivable that the reabsorption of water at such time might in itself produce sufficient change in viscosity to account for the final picture. However, if sphincter spasm following chlorpromazine occurs with anything like the frequency it does with morphine, one must still account for this relatively infrequent occurrence of jaundice or assume that additional complicating factors must be present to produce the disorder.

Histologically the findings resemble those seen in jaundice following methyl-testosterone administration. Oddly enough jaundice has not been reported following the use of testosterone proprionate. It has been shown that the metabolic pathway manifested by the formation and excretion of creatine differs in patients taking the methyl derivative of testosterone from those using testosterone proprionate. This suggests the possibility that an intermediary metabolite produces the abnormality.

The principal metabolite of chlorpromazine is sulfoxide. It would be of interest to know whether or not in jaundiced patients the quantity of the various metabolic breakdown products are altered. Conceivably the ability of such patients to resolve their jaundice while continuing to take the drug or to resume drug therapy without a recurrence of jaundice once it has subsided, might be explained by the ultimate development of a new metabolic pathway for the drug, rather than a desensitization phenomena or increased excretory pressure in the liver.

Our knowledge is well summed up by a sentence I noted in a discussion of the effect of chlorpromazine on hepatic function in which the author stated that, "While not a specific hepatotoxin the drug is capable of eliciting unpredictable hepatic responses in susceptible patients."

Clinical Applications of Continuous Pressure Recordings from the Common Bile Duct*

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The studies reported by the authors, and those projected in the future may cast light on a number of clinical problems poorly understood at the present.

Introduction

THE AUTHORS have recently described a new method for the accurate recording of naturally occurring pressures in the human common bile duct, employing a strain gage manometer. These recordings were made in postoperative patients with indwelling T-tubes. The results of the study demonstrated that this method can be used in human subjects without danger or discomfort. Earlier studies[1-3] on animals have employed water manometers, in which the risk of infection is implicit because perfusion of fluid into the T-tube is necessary. Furthermore, this method measured resistance to flow and not naturally occurring pressures. With the use of a strain gage manometer and suitable recording apparatus only a small displacement of volume is required to register pressure changes. This method, therefore, measures more accurately the naturally occurring pressures within the common duct. The equipment to perform this procedure is now available in most large hospitals which are equipped with cardiorespiratory laboratories. As the use of such equipment becomes more commonplace, probably further uses will be found for recording processes in various gastrointestinal studies.

Observations of Pressure Variations

Pressure recordings during the basal state were found to range from 70 to 220 mm. of water. Several types of pressure waves were observed during the resting fasting state (Fig. 1). Regular symmetrical waves occurred synchronously with respiration. These were of a magnitude of 20 to 50 mm. of water depending upon the depth of respiration. Deep inspiration produced waves as large as 75 mm. of water, whereas the Valsalva maneuver produced a high sustained pressure of over 350 mm. of water, which, in most instances, exceeded the limits of the recording equipment. Another type of wave observed was a sharp rapid wave of 2 to 5 mm. that occurred synchronously with the pulse. All of these waves are believed to reflect variations of intra-abdominal pressure.

It has been observed that all of the waves previously described in studies of small bowel motility[4] were also present in our recordings of common duct pressures. Consequently, the conclusion was drawn that these waves are pressure changes which are transmitted from the duodenum and the intraduodenal portion of the common bile duct. Previous reports have considered these to represent primary peristalsis of the common duct.[3,5,6] The common duct proximal to the intraduodenal portion lacks significant musculature to effect a pressure change of 300 to 400 mm. of water. These variations of pressure within the common duct have been observed both in the presence and absence of an intact sphincter and, in one instance, in a patient after cholecystojejunostomy.

Waves of motility can be produced in the small intestine by ingestion of food and by administration of certain drugs. Similarly, in the common bile duct variations in pressure can be obtained, and typical waves of Type I, II, or III can be produced by administration of food or paregoric (Figs. 2 and 3, and

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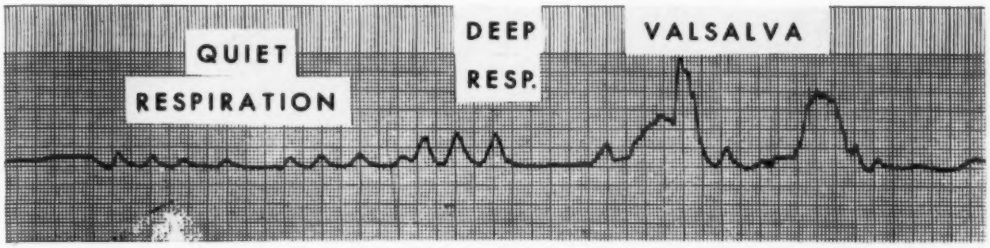
FIG. 1



Variations in common duct pressure as recorded by a strain gage manometer during the resting fasting state. These waves are believed to reflect variations of intra-abdominal pressure. Heavy time lines occur every two seconds.

Table 1). These waves can be abolished by administration of amyl nitrite.

Clinical Application of Pressure Recordings

Several patients with uncomplicated cholecystitis were studied and continuous pressure recordings were made from the indwelling T-tube in the common duct. Another group of patients with pancreatitis were similarly studied. It was apparent that the tracings of these two groups of patients were qualitatively and quantitatively different, and it is our impression that pressure recordings may be of differential value in determining whether obstruction of the common bile duct is organic or spastic in nature. Two case summaries are presented that illustrate this point.

TABLE 1

EXAMPLES OF COMMON DUCT PRESSURES IN PATIENTS WITH AND WITHOUT OBSTRUCTION OF THE COMMON DUCT DUE TO PANCREATITIS

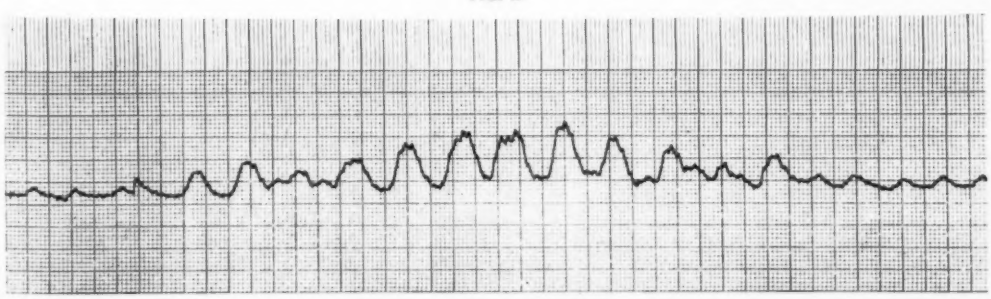
	Basal Pressure	*Postprandial Pressure*	*Type Waves Present*	*Effect of Amyl Nitrite*
Normal (M.P.)	110	270	I, II, III	300—120
Pancreatitis (P.M.)				
1st tracing	220	260	None	250—250
2nd tracing	160	170	None	150—150

Pressure expressed in millimeters of water and referred to point of exit of the T-tube.

Case 1. A 64 year old white woman, had a history of constipation and lower abdominal cramping for several years. During the previous two to three years she had had occasional episodes of right upper quadrant pain which were never severe enough to require opiates for relief. X-ray survey showed radiopaque stones in the gallbladder. At operation the gallbladder was found to be thick-walled and to contain stones. The common duct appeared normal, but when incised a small stone was found. The pancreas was grossly normal. Cholecystectomy, choledochostomy, and appendectomy were done. The postoperative course was uneventful and a postoperative cholangiogram showed no abnormal findings. A pressure study was done two weeks after the operation (Fig. 3 and Table 1).

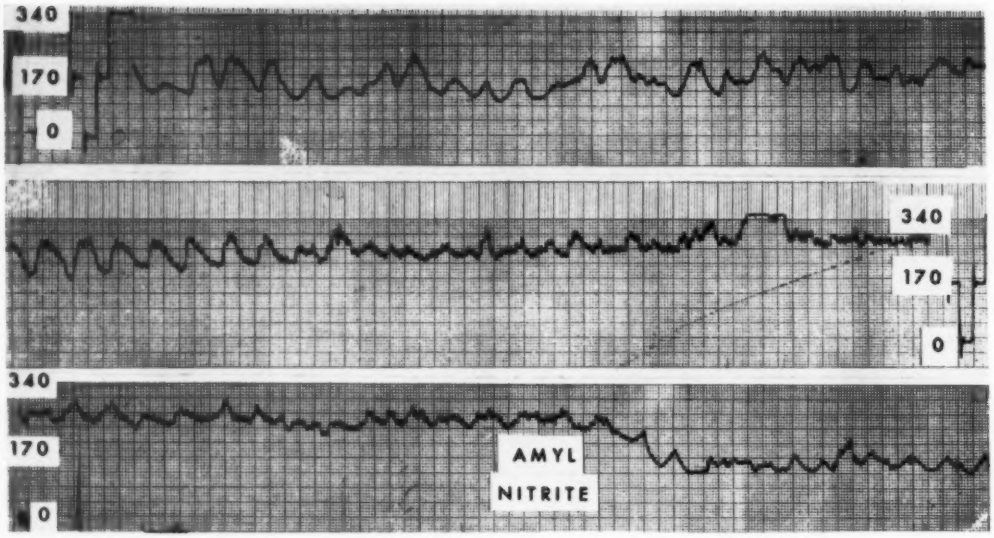
Case 2. P. M., a 65 year old white woman, was first seen in July, 1955, after the sudden onset of constant severe upper abdominal pain with vomiting, which required injections of opiates for relief. Similar bouts of pain recurred in September, 1955, and again in March, 1956. In April, 1956, a second gallbladder study showed a nonfunctioning gallbladder. Results of the routine laboratory studies were essentially normal, with the exception of the serum amylase (normal 40 to 100), which was 220 mg. per cent on

FIG. 2



Variations in common duct pressure as recorded by a strain gage manometer in a patient without pancreatitis and following administration of paregoric. This tracing represents Type I waves surmounted on a slower Type II wave. These waves are believed to be identical to motility waves of the duodenum.

FIG. 3



Variations in common duct pressure as recorded by a strain gage manometer (Case 1) following the administration of paregoric. This is a continuous recording of a Type III wave with Type I and II waves surmounted. The numbers represent standardizations of pressure expressed in millimeters of water. Note prompt fall in pressure on administration of amyl nitrite.

March 19, 1956; on March 21 it was 268 mg., and on April 8, 90 mg. per cent. At operation the gallbladder was thick-walled; the common duct contained several small stones; and the head of the pancreas was thickened but showed no fat necrosis. An oval firm mass 3 cm. in diameter was found in the body of the pancreas. Cholecystectomy, choledochostomy, partial pancreatectomy, and appendectomy were done. The pathologic diagnosis was benign cystadenoma of the pancreas, acute and chronic pancreatitis, and mild cholecystitis. The postoperative course was essentially uneventful. The first pressure study was done on the 21st postoperative day, and the second on the 40th postoperative day, at which time the patient was asymptomatic and was eating reasonably well (Table 1).

These two cases are typical examples of pressure differences obtained in patients with and without obstruction of the common bile duct due to pancreatitis. It is noted that the normal resting, fasting pressure ranges from 80 to 130 and that in the group of patients with pancreatitis the initial pressure range was from 130 to 220. Administration of amyl nitrite did not reduce the basal pressure. Administration of paregoric or feeding resulted in an increase of pressure in most instances from 100 to 250 above the basal pressure level in the normal group. In the presence of pancreatitis, however, this increase in pressure was less pronounced. Waves of fluctuating pressure of Types I, II, and III were observed in normal patients, but in patients with pancreatitis waves of Types I and II were notably absent. When subsequent observations were made of patients with pancreatitis in which the disease process appeared to be subsiding, these differences were observed to resolve progressively toward normality.

It would seem that pancreatitis serves as an obstructing mass which increases the pressure within the bile duct. In addition, this obstructing mass appears to interfere mechanically with the transmission of the pressure variations within the duodenum to the common duct.

Proposed Studies

The use of this new recording technic offers a method of study and re-evaluation of the effects of opiates, antispasmodics, and blocking agents on biliary pressure. Studies to differentiate organic and spastic obstruction could be used more extensively. Several surgical procedures of questionable value could be further explored with this technic, particularly caudal decompression of the pancreas and sphincterotomy. Such studies could be extended to evaluate pressures within the pancreatic duct. Finally, in our opinion, this

method of recording pressure has definite clinical applications and may add significantly to present knowledge and understanding of the physiology of the digestive tract.

Summary

Continuous pressure recordings with a strain gage manometer were obtained in patients with a T-tube in the common duct. The various causes of variations in pressure are considered. Tracings in patients with known pancreatitis were qualitatively and quantitatively different from those recorded in patients without pancreatic disease.

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Discussion (Abstract)

Dr. William W. Shingleton, Durham, N. C. I would like to congratulate Drs. Kelsey and Beard on their development of an improved method of obtaining common bile duct pressures in postoperative unanesthetized patients. The accurate measurement of physiologic pressures in the pancreatic and common bile ducts has been most difficult in the patient. Various methods of recording pressures in animals and man have been previously described, but none has been entirely satisfactory. The most commonly used method in the past has been that of creation of a fistula, such as with a T-tube, in the common duct and perfusion of a solution through the fistula with a water manometer to measure resistance of flow. We have used this method in both animal and human experiments. Dr. Kelsey's use of a strain gage manometer for recording pressures within the common duct represents a technical advance in the solution of the problem. It should be pointed out, however, that the recording of pressures within the bile duct of postoperative patients with indwelling T-tubes is subject to many variables and does not necessarily represent physiologic pressures in the common duct. These patients have had their gallbladders removed; this organ participates in the emptying mechanism of the biliary tract. There is much evidence to suggest that bile duct pressure rises after cholecystectomy, leading to dilatation of the common duct. The amount of trauma incident to exploration of the common duct would most likely affect pressures in the duct for a variable period of time. Studies by Bergh indicate that spasm of the choledochal-duodenal sphincter mechanism may exist for several weeks or months after removal of stones from the duct. The emotional state of the subject under study may influence the results obtained. Disease in viscera adjacent to the common duct, such as pancreatitis, undoubtedly will influence the results obtained.

The need for more accurate studies on biliary tract pressures is apparent from both the physiologic and clinical standpoint. The importance and the mechanism of the sphincter of Oddi in emptying of the biliary tract in the human need more precise definition. Dr. Kelsey's findings suggest that the musculature of the duodenal wall may be of more importance than the sphincter of Oddi. The relative importance of the neurogenic and hormonal control of emptying of the biliary tract needs elucidation. Using the perfusion method of determining bile duct pressure we found evidence of neurogenic control of the choledochal sphincter in cats and dogs, but in similar studies in the human, using drugs with selective action on the component parts of the autonomic nervous system, we found no consistent pattern of neurogenic control of sphincteric resistance.

There are several clinical problems which would be clarified by reliable studies on biliary tract pressures. Outstanding among these is the relationship between biliary tract disease and pancreatitis, between the biliary tract and coronary artery disease. Other problems for study are biliary dyskinesia, the so-called postcholecystectomy syndrome, and the effect of operations on the sphincter. A further analysis of the effect of various drugs on biliary tract pressures in health and in disease is needed. Dr. Kelsey's finding of a distinctive pressure difference in patients with cholecystic disease, with or without pancreatic disease, might well provide an opportunity to evaluate therapy of pancreatic disease. In addition, further studies on biliary tract pressures are needed in patients without biliary disease and with the gallbladder intact. I feel sure that with improved technics for study many of these perplexing problems will be solved.

Fate of Women with Positive Cervical Cytology*

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This is a most interesting follow-up study of women shown previously to have a positive cytologic cervical smear.

AT THE TIME a full-time Department of Obstetrics-Gynecology of the Jackson Memorial Hospital and University of Miami School of Medicine was established in June, 1955, 5,473 cytologic studies of the cervix had been done. To appraise the usefulness of this diagnostic tool and to provide a service for the women who depend on this hospital for care, the records of all of the women with positive cytologic findings were collected into a Positive Cytology Registry. These case records were brought up to date insofar as was possible with an intensive case-finding effort in July and August, 1956. This paper is an account of the fate of the women who had cytologic studies of the cervix which resulted in a positive report. Some comments will be made on our current management of women with this problem.

Methods

The smears have been made from a surface-cell scraping of the cervix with a wooden spatula. Two slides were prepared at each examination. The reports of cytologic examination that have been in use and a comparison of our classification with that of Papanicolaou are given in table 1. Our grades which are called (a) "slightly suspicious for cancer cells," (b) "suspicious for cancer cells," and (c) "highly suspicious for cancer cells" are here referred to as "positive" and when they were thus reported have been included in our Positive Cytology Registry.

TABLE 1

CYTOLOGY CLASSIFICATIONS

Jackson Memorial Hospital	*Papanicolaou*
No cancer cells seen	Class I, Negative Absence of atypical or abnormal cells
No cancer cells seen Advise repeat at 3 mos.	Class II, Negative Atypical cells present but no evidence of malignancy
Slightly suspicious for cancer cells. Repeat in 3 mos.	Class III, Suspicious cells suggestive of, but not conclusive for, malignancy
Suspicious for cancer cells. Advise repeat smear or biopsy	Class IV, Positive Cells strongly suggestive of malignancy
Highly suspicious for cancer cells. Advise biopsy	Class V, Positive Cells conclusive for malignancy.

Some Generalizations on Results

In the period being surveyed, dating from the first cervical cytologic study in March, 1952, to July 1, 1955, there were 169 women with positive smears among the 5,473 examinations made. In July-August, 1956, 85 of these women (50 per cent) were located and their follow-up brought up to date. These are the women with "completed follow-up." The remaining 84 were lost to follow-up at that particular time, but are being sought in a continuing case-finding effort. The 85 women with completed follow-up will provide us with the most valuable comments we can make, although some conclusions can also be drawn from the group with an incomplete follow-up.

The distribution of the positive cytologic diagnoses among a group of 85 women who are described as having a "completed follow-up" is listed in table 2. Thirty-five were designated as "slightly suspicious," 26 were "suspicious," 20 were "highly suspicious," and in 4 the grade of positiveness was not recorded.

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TABLE 2

DISTRIBUTION OF POSITIVE CYTOLOGY DIAGNOSES COMPLETED FOLLOW-UP OF PATIENTS

Slightly suspicious	35
Suspicious	26
Highly suspicious	20
Not recorded	4
Total	85

Thirty-three of all the women with positive cytology were eventually found to have invasive squamous cell carcinoma of the cervix. Since we have data available only on the number of cytologic examinations made and not on the total number of women studied, we do not know the incidence of carcinoma among the women in our clinic. There was one case of carcinoma of the cervix to 166 examinations or 6.1 cases per thousand. Intra-epithelial carcinoma is probably about one-half as frequent as invasive carcinoma. Among the 5,473 studies there were 16 women with intra-epithelial carcinoma. Since these 5,473 examinations stem from routine admissions to a gynecology clinic, the cases of cancer cannot be considered as cases discovered by this technic. Even though there was no visible lesion on the cervix, the routine use of cytodiagnosis did reveal some cases of unsuspected cancer, 3 with invasive carcinoma of the cervix, 3 intra-epithelial carcinomas of the cervix and one case of carcinoma of the ovary.

The diagnoses of the women with positive cytology and completed follow-up are listed in table 3. Among these 85 women the most prominent diagnoses were invasive carcinoma in 25 women, cervicitis in 21, and intra-epithelial carcinoma in 9.

Age. Despite some concentration of elderly people in Florida, there was a remarkably larger proportion of younger women among our patients with positive cytologic findings. Approximately one-third of all of our patients with positive results were under 30 years of age. This is interesting in view of the fact that Erickson and associates[1] found in the Memphis survey that the peak incidence of intra-epithelial carcinoma was from 30 to 34 years and invasive carcinoma from 50 to 54 years.

TABLE 3

CHIEF DIAGNOSES COMPLETED FOLLOW-UP—POSITIVE CYTOLOGY

No diagnosis	28
Carcinoma, cervix	25
Cervicitis	21
Intra-epithelial carcinoma	9
Cancer, endometrium	1
Cancer, ovary	1
Total	85

The tendency for the average age of patients with intra-epithelial carcinoma to be lower than the average age for patients with invasive carcinoma has been reported a number of times. Among the patients at the University of Miami we find the same trend. Thirty-seven is the average age for women with intra-epithelial carcinoma at the time of diagnosis and 47 years for the invasive form. The implication is that here is evidence that intra-epithelial carcinoma is a precursor of the other. The youthfulness of our patients with positive cytology may be an indication, if duplicated elsewhere and in the future at the University of Miami, that just as invasive carcinoma may be preceded by intra-epithelial carcinoma, so may some years of exfoliation of abnormal cells precede intra-epithelial carcinoma.

For another reason our experience does not encourage the placing of a lower limit on the age at which cytologic screening can be useful. In 1956, we are finding one positive smear in every 35 cases studied. This represents an increase in our incidence of positive smears and must be due in part at least to the addition to our cancer-detection program of all of the patients admitted to the obstetric clinic. It seems that in the future we can anticipate that the average age of women with positive cytology may be even less than is being reported at this time.

Race. In both the completed follow-up and incomplete follow-up groups the number of white patients with positive cytologic results was almost exactly the same as in the non-white patients. In the attendance at out-patient clinics we have a slight majority of non-white patients.

Fate of Women with Positive Cytology

Of the 85 women with completed follow-up, 76 are alive and 9 are dead. Three died of carcinoma of the cervix, one of carcinoma of the ovary, 2 of cancer of the stomach, 2 died of medical diseases unrelated to cancer, and one died of an unknown cause.

Forty-three of the 85 women (51 per cent)

had false positive cytology reports. They were falsely positive in the sense that no cancer, invasive or intra-epithelial, had appeared by July-August, 1956. To know whether these women will ultimately be labeled as "false positives" will need a number of years to provide the answer. This answer, we hope, will be provided by the continuing activity of the Positive Cytology Registry in following these patients. There are a number of other questions we hope to answer in the future with the assistance of this agency. Does the fact that a woman had a positive smear and no disease was demonstrable, or that subsequently there was a change to a negative smear, mean that there is an increased risk of developing cancer in the genital organs or elsewhere in the future? How accurate were the diagnostic studies in themselves? How effective was the office treatment of vaginal or cervical disease in accomplishing this improvement in the cytology-based prognosis? These are all questions we must keep in mind when we plan the care of patients with positive cytologic findings. The fact that we cannot answer them yet should guide us to a management of caution, conservatism and a prolonged, careful follow-up of the patients.

Eighty-four of the entire 169 women with positive cytology could not be found in July-August, 1956. Four of these women had records of two or more smears that showed a progression in the degree of positiveness. All of these women are being energetically sought by the personnel in the Positive Cytology Registry. The urgency of a thorough search is emphasized by our knowledge that eight of these women had invasive carcinoma of the cervix and seven had intra-epithelial carcinoma. Besides this service function that the Registry will perform it will produce valuable data on the natural history of women who exfoliate abnormal cells.

Spontaneous Disappearance of Positive Cytology Tests

Among the 85 patients with positive cytology and completed follow-up there were 39 women in whom the cytologic test became negative without the benefit of hysterectomy or radiotherapy. These patients have been followed from 11 to 52 months, with an average of 32 months and a median of 31 months. We plan to follow indefinitely this very interesting group of women, and others we may accumulate in the future, to see if we can learn something from them. Does this temporary state of positiveness mean that they are destined to develop cervical cancer later, or cancer in another area of the body? What factors could have produced or reversed these positive smears? Will the positive smears recur later? A small majority of these women, 62 per cent, had smears that were classed as "slightly suspicious." Ten of the remainder were "suspicious," and 5 were "highly suspicious."

There was a wide variety of diagnoses among the cases which had a spontaneous disappearance of positive findings. In too large a number, 20, no tissue diagnosis was ever made. There was one instance of intra-epithelial carcinoma and it is now 24 months since the diagnosis was made by cone biopsy. Fifteen had cervicitis, one a cervical polyp, and 2 invasive carcinoma. The 2 cases of invasive carcinoma will be elaborated upon.

Case 1. M. B. had three slightly suspicious smears in 1952 and 1953. In November, 1954, no cancer cells could be found although the cervix was described as having a "few erosions." It was reported by the Bureau of Vital Statistics that she died of carcinoma of the cervix 6 months later, without being seen by us in the interim. We will have to assume that the negative smear was a "false negative" test.

Case 2. C. S. had a stage II carcinoma of the cervix diagnosed in December, 1954, while in the first trimester of pregnancy. She refused treatment of the carcinoma. In April, 1955, she was delivered and then treated with radium; the stage now was IV. She almost died of hemorrhage twice, in November and December, 1955. In December, 1955, treatment was started with triethylene thiophosphoramide, and although her pelvis is still filled with a frozen mass, cytologic study and biopsy are consistently negative. She feels very well and has no bleeding. The large crater that once replaced her cervix has become a tiny opening. This is the only encouraging result we have had in an experience of 18 cases of carcinoma of the cervix treated with triethylene thiophosphoramide.

What treatment may these 39 women have had which could possibly be given credit for the reversal of the cytologic reading? One woman became negative after the removal of a benign cervical polyp. Because all tests have been negative since, 14 were apparently relieved of the threat of cancer by the diagnostic operation of cone biopsy and fractional curettage of the cervical and uterine cavities. The permanence of the reversal which followed these operations will eventually be determined as we continue our follow-up of these patients. Since July, 1955, we have ac-

cumulated more patients who have had only cone biopsy and curettage, and altogether the fate of these patients will contribute greatly to our knowledge of the natural history of the women who produce abnormal cells.

Others among the cases having a spontaneous disappearance of positive smears is one patient who had a punch biopsy. Twenty-three women had no treatment. No woman in this series had cauterization of the cervix, because cauterization was not a popular procedure in the clinic at that time. Since the time covered by this study cauterization has become routine treatment in women having a cervical lesion proved to be benign by biopsy and who show only a minor degree of atypism in the smear.

These reversals in the smears from positive to negative occurred despite the fact that between the first positive cytologic report and the last negative one (July-August, 1956), 6 of the patients have had 7 pregnancies.

Such a large number of women with spontaneous disappearance of the positive cytologic smears received no treatment because of confidence that the progress of the case could be controlled simply by repeated cytologic examinations. We believe this confidence was unwarranted and we now pursue these cases of definite positive cytology more vigorously, if less bravely, with punch biopsies, cone biopsies and fractional curettage.

There were also 4 cases of spontaneous disappearance of positive smears among the women in whom follow-up was incomplete. These women were observed for periods of 10, 10, 9, and 4 months, between the first positive smears and the negative smears. All had cone biopsies before the reversal of positive smears. They have been lost to our observation and at the moment we are unable to find them.

The Effect of Pregnancy on Cervical Smears

The relation of pregnancy to the discovery of abnormal cells originating in the cervix is provoking much interest today. We have reason to believe that pregnancy can cause or heighten these dangerous alterations in the cells of the cervix. Questions yet to be answered concern the importance, the prevalence, and duration of these changes. It is generally concluded that suspicious cells can sometimes disappear in the postpartum weeks. We have had some cases in which the test did not become negative. The factor of pregnancy as a precursor or inciter, although a weak one, to carcinoma of the cervix is all too obvious. Of the 169 patients in our Positive Cytology Registry only 6 are nulligravidas, 3 of whom we have in our completed follow-up file.

Among the 85 patients with completed follow-up, 12 have had 17 pregnancies since the first cancer cells were found on smears. These patients have been followed on an average of 36 months and as yet we can draw no conclusions from this group. We will wish to know if the pregnancies accelerated the change from normal cervical cells to abnormal ones. These patients include one with invasive carcinoma and 2 with intra-epithelial carcinoma. All patients are alive and well. Included among these patients are 6 women who have had a "spontaneous" disappearance of the positive cytologic tests.

In November, 1955, which postdates the time covered in this report, we began to obtain cytology tests on all admissions to the Obstetric Clinic. Before that date this test was done only on selected obstetric cases, in particular those who had an admission to the Gynecology Clinic for the purpose of the diagnosis of pregnancy. With the augmentation of the number of pregnant patients who have this examination there appears to be a not unanticipated increase in diagnostic problems of cervical disease. We suspect that a careful analysis will reveal that we are getting more abnormal smears from pregnant women than we would from a comparable age group of nonpregnant women.

We do not have enough cases as yet to make any dogmatic statement about the spontaneous regression of abnormal cells after the pregnancy is over. Among the 85 patients with positive cytology smears who have been completely followed up, were 7 patients who were pregnant at the time of the first positive cytologic test; there were 4 such women in the group lost to follow-up. Two of the completed follow-up group had intra-epithelial carcinoma and one had invasive carcinoma; one of the women with intra-epithelial carcinoma had no visible lesion and we owe the early diagnosis to the cytologic examination. The records of our 84 incompletely followed

patients promise to provide us with more data on the effect of pregnancy when these women can be traced. There are 14 women in this group who have had at least 17 pregnancies. One of these women had invasive carcinoma and 2 had the intra-epithelial form.

Because we are able to "sell" postpartum clinic visits to many women who have had no antepartum care, we have a large number of opportunities to see the results of cytologic examinations in postpartum women. We now do a cytologic examination on each first postpartum visit and this procedure is providing us with a rich, although perplexing, source of patients with positive cytology. We have some reason to suspect that at six weeks postpartum a number of women still have a positive cytology induced by the pregnancy and that with time the positive findings will disappear, at least in some women. Other factors besides time are undoubtedly at work,—for example, the cone and punch biopsies we obtain on these women and the subsequent cauterization when it is indicated.

Among the 85 positive cytology cases with completed follow-up, 8 were first discovered to have a positive cytologic test at the postpartum visit. Two of these had invasive carcinoma and 3 had intra-epithelial carcinoma. Another 14 women, unfortunately lost to follow-up, were also first diagnosed at the postpartum visit. These women have disappeared and continue to be a challenge to our case-finding efforts. A very much larger number of women had atypical cells on their smears, but cannot be classified as yet as having a positive test. We expect some day to be able to explain how long their atypical cells lasted and what the fate of these women is. Our experience with the cytologic studies at the postpartum visit demonstrates the value of this visit as a cancer-detection effort as well as a cancer-prevention measure.

Summary and Conclusions

The fate of 169 women with positive cervical cytology was investigated. The longest follow-up on these patients was about three years and 9 of these women are now dead. Thirty-three of these women had invasive carcinoma of the cervix and approximately one-half, 16 women, had intra-epithelial carcinoma.

Our experience does not support the placing of a lower age limit at which cervical cytology can be useful, nor does our experience indicate that obstetric cases should be excluded from this type of study. One third of all our patients with positive cytology are under 30 years of age. The average age of all women with positive cytologic smears was lower than that of women with intra-epithelial carcinoma or invasive carcinoma.

Only 6 of the 169 women in this study were never pregnant. The antepartum and postpartum clinics are a rich source of positive smears. Many of these tests become negative, apparently with the assistance of time and biopsies.

Positive cervical smears have disappeared spontaneously. Others have never reappeared after cone biopsy of the cervix. All should be followed indefinitely.

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Discussion (Abstract)

Dr. James A. Dusbabek, Washington, D. C. First of all, I would like to congratulate Dr. Ferguson for his most excellent presentation and for his thoroughness in establishing a good follow-up study of the cases with positive cytology.

He should be commended for insisting on a routine cervical cytologic study on all patients admitted to the Gynecology Clinic. Routine cytologic examination on all obstetric patients, however, presents a different picture. There is a higher percentage of abnormal smears in this group which is understandable, because we seem to find more erosions and abnormal looking cervices in the pregnant patient. In our own Warwick Cancer Detection Clinic here in Washington, of 709 consecutive smears sent in by private physicians only 29 were associated with pregnancy; 25 were from pregnant and 4 from postpartum women. Of these, 22 were class II and 5 were class II with atypical cells. On questioning several of the obstetricians in this area, very few do routine cervical cytologic examination in pregnancy, and in my own series of over 1,600 cases very few were done on pregnant patients.

Why do we avoid doing smears on these patients? For one reason the high percentage of abnormal smears or false positives cause a lot of unnecessary worry, and in the absence of a suspicious or actual lesion repeated smears during pregnancy would be of little value. If, however, there is a suspicious lesion, cytologic study and biopsy would be done and proper treatment given at the appropriate time. Cytologic study in the postpartum patient is being done by many obstetricians, and possibly the best time to do these is at the three month postpartum examination.

I can see no harm in allowing a patient to become pregnant who has had a positive smear and who has subsequently become negative. Closer observation of such a patient is certainly advocated.

It is interesting to note that of 85 patients with positive smears 51 per cent became negative. This, more or less, parallels my series. The reversal from positive to negative is interesting. Many of these occur following removal of endocervical polyps, simple conization or multiple biopsies of the cervix, or on the clearing up cervical erosions or infections. A statement is made that none of these cervices were cauterized. It is my policy to cauterize or fulgurate some cervices that show erosion if cytologic smears or biopsies are negative, and I am glad to hear that Dr. Ferguson is now doing this in his clinic.

He has pointed out that in too large a number (20 cases) no tissue diagnoses was ever made. I am sure these must have been seen before he became Chairman of the Departntent. Not to do a conization or biopsy when a highly suspicious smear is reported is certainly negligent. One may just as well not bother with a smear in the first place.

All patients on whom suspicious cytologic findings are reported should be further studied. The class II patients should be studied by repeated smear, and the class III by cone biopsy, and curettage of the endocervix and uterus to determine whether or not there is any evidence of malignancy. If no malignancy is found, scheduled follow-up smears are necessary over a period of years even though subsequent smears are negative.

This is why a Positive Cytology Registry is important. In private practice it is a simple matter to review one's list of positive cases and notify those who do not come in on scheduled appointments. However, in large clinics there are many problems which make it difficult to keep a close check on these patients. In hospital clinics there is generally a large number of patients seen, as a rule, by a rotating house staff. There is not the close relationship with the patient as in private practice, and therefore many of the patients are certain to be lost if they are not followed closely. A Positive Cytology Registry handled by a responsible member of the Department or Social Service Department will certainly prevent the loss of most of these patients.

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Postmenopausal Bleeding:

A Re-evaluation of an Old Problem

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The problem of postmenopausal bleeding is troublesome and worrisome. This thoughtful review of case material will answer some of the questions which arise.

Introduction

THE SUBJECT OF POSTMENOPAUSAL BLEEDING has been the theme of many publications. The pathologic lesions responsible for this symptom have frequently been recorded and the high incidence of malignancy has been stressed. Due to the increased use of estrogens and resultant bleeding, as well as other factors to be discussed later, the percentage of malignancies has decreased. Nevertheless, the dictum that postmenopausal bleeding should be regarded as evidence of malignancy until proven otherwise is still appropriate and wise. The present study was undertaken to answer several questions which have been given little consideration in the medical literature but which have great practical significance. These are as follow:

1. How frequently does postmenopausal bleeding recur after an initial curettage which fails to reveal malignancy?
2. How often is the basic and often serious disease missed at the initial curettage?
3. In the patient with benign disease, how often is definitive therapy ultimately required?
4. How long should one persist in diagnostic and minor surgical procedures in the face of recurrent bleeding?

Material

We have arbitrarily included in this series cases in which bleeding has occurred one or more years after the last presumably normal period. We recognize the confusion in the literature on this point, but for practical purposes a definite time interval must be decided upon and one year would seem reasonable.

From January 1, 1946, through December 31, 1951, 574 cases of postmenopausal bleeding were evaluated on the Gynecological Service of the Johns Hopkins Hospital. All cases of genital bleeding are included. We have purposely included not only those cases in which the bleeding arose from the uterus but also those in which the bleeding originated in the vagina, urethra and vulva. Often the patient is uncertain of the source of the blood; hence for practical reasons all bleeding from the region of the genital outlet should be included. It should be stressed, however, that the finding of senile hemorrhagic changes in the urethra and vagina does not eliminate the necessity of study of the remainder of the canal. Only those patients who had undergone a natural menopause are included. Hemorrhage after menopause induced surgically or by irradiation constitutes a different problem and has been considered separately.[1]

Pathology

In table 1 the lesions found to be associated with postmenopausal bleeding are classified according to their benign or malignant nature and anatomic location. Over the years the causes of postmenopausal bleeding have remained practically constant but there have

TABLE 1

PATHOLOGIC DIAGNOSIS IN 574 PATIENTS WITH POSTMENOPAUSAL BLEEDING, 1946-1952

	Cases	*Per Cent*
No demonstrable disease	222	38.6
Corpus, benign	148	25.7
Cervix, benign	56	9.7
Corpus, malignant	53	9.2
Vaginal lesion, benign	45	7.7
Cervix, malignant	34	5.9
Ovary, malignant	6	1.0
Urethral lesion, benign	5	0.8
Ovary, benign	3	0.5
Vulvar lesion, benign	1	0.1
Vulvar lesion, malignant	1	0.1
Total	574	99.3

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been variations in the relative incidence of the lesions, dependent upon several factors which will be discussed later.

No attempt will be made to analyze in detail the exact pathologic lesions associated with postmenopausal bleeding since that has already been done by many authors and such is not the purpose of this paper. Attention will be called to some points which have a direct bearing upon the questions proposed in the introduction of the paper. More than one in four patients (25.7 per cent) bled because of benign disease of the corpus uteri. Other benign conditions accounted for 18.8 per cent of the total series. Thus, 44.5 per cent of the entire group was found to have a demonstrable nonmalignant lesion as a cause for the complaint. If to this figure the 38.6 per cent is added in which malignancy was excluded but no acceptable explanation was found for the bleeding, the total incidence of benign cases among the 574 patients becomes 83.1 per cent. This is to be contrasted with an incidence of nonmalignancy of only 47 per cent found by one of us in 1937.[2]

Why have these figures shown such a decided change? There are several reasons. In the first place, both patients and doctors are more alert to the possible significance of this symptom. Hence, more women are investigated for slight bleeding and are studied earlier. This would naturally increase the incidence of the benign cases since in many of these the bleeding disappears spontaneously. In recent years there have been an increasing number of women who receive estrogens after cessation of menstruation. In a certain number of these bleeding is thus artificially induced. Sometimes this is associated with hyperplastic changes in the endometrium and in others it is not. This probably represents a larger group than is shown in the above figures because women often fail to give the facts spontaneously regarding this therapy and house officers often fail to ask the specific question. These two reasons, earlier and more frequent investigation, together with estrogen therapy, are probably the major factors in the increased incidence of benign bleeding.

Finally, we have encountered a definite decrease in the number of cervical cancers treated in postmenopausal women per unit of time. Our total number treated per year in all ages has not decreased during this period. The only explanation available is that cervical cancer is being diagnosed and treated earlier. An analysis of our cervical cancer cases indicates a gradual increase in the number of cases falling into stages O, I and II, and a decrease in the more advanced cases. In fact, the gradual improvement in five year salvage which we have seen during the past several years would appear to be on this basis. This seems to confirm our explanation of the decrease in the incidence of postmenopausal cervical cancer.

Malignancies of the corpus have not shown this decrease. Whereas in the study made in 1937 cervical cancer occurred approximately twice as frequently as cancer of the corpus, in the present series the latter were more frequent than those in the cervix, the ratio being five to three. This trend may be explained in part on the basis of the decrease in cervical cancer in this age group, but increased longevity may also be a factor. Many more women are living to the age when fundal malignancy is prevalent.

Treatment

In those cases in which malignancy was diagnosed at the time of the first curettage and cervical biopsy appropriate definitive therapy was carried out. In this study we are chiefly concerned with patients in whom malignancy was not diagnosed at the time of the first curettage. As shown in table 2, in 7.2 per cent major surgery was deemed necessary initially. The indications for operation were symptomatic myomata, benign ovarian lesions, and in several instances varying degrees of uterine descensus. In addition, 20 patients were operated upon for some incidental condition at the time of curettage. These operations were, for the most part, vaginal plastic procedures.

The ultimate fate of the patients in whom no malignancy was found at the first curet-

TABLE 2

TREATMENT OF BENIGN CASES AT INITIAL STUDY

	Cases	*Per Cent*
Dilatation and curettage, polypectomy, etc.	410	85.3
Hysterectomy	35	7.2
Repair procedures with dilatation and curettage	20	4.1
Radium	14	2.9
Vulvectomy	1	0.2
Total	480	99.7

tage is of prime importance in guiding us subsequently in the care of patients with postmenopausal bleeding. To determine this, letters were sent to 444 patients who did not have a major operation done at the time of the initial curettage. Replies were received from 333. The lapse of time from the initial curettage to the inquiry varied from one to eight years. As might be expected in this age group a certain number of these women had died; this was true in 19 instances. No further bleeding had occurred in 259, or 77.8 per cent. Seventy-four, or 22.2 per cent, did bleed subsequently. The treatment of this group is presented in table 3. In 18, or 5.4 per cent, the bleeding subsided spontaneously. In 56 patients, or 16.8 per cent, subsequent bleeding occurred which required further treatment, but in only 3 of these was malignancy found. In the remaining 53 women simple curettage proved to be sufficient therapy in 40; in 13, hysterectomy was done for myomata, recurrent pyometra or postmenopausal endometrial hyperplasia.

The histories of three women (0.8 per cent) who eventually proved to have malignancy are of sufficient importance to warrant brief summaries.

Case 1. B. B., a 53 year old white woman, 36 months postmenopausal, had her first episode of mild, intermittent bleeding. D & C was performed in 1950 and a diagnosis of myomata uteri and benign endometrium. Recurrent bleeding with a second curettage occurred within a year, the diagnosis, endometritis. Hysterectomy was done because of gross disease and recurrent bleeding. *Final diagnosis* was adenoacanthoma, fundus uteri.

Case 2. H. B., a 62 year old white woman, had a D & C and repair done in 1945, with a pathologic diagnosis of benign endometrium. Because of recurrent bleeding a D & C was again done (1949). *Final diagnosis* was carcinoma, fundus uteri.

Case 3. C. W., a 50 year old negress, 3 years postmenopausal, had intermittent and moderate bleeding (first episode). A D & C was performed in 1950 with a pathologic report of benign endometrium. A diagnosis of large myoma uteri was made but major surgery was not done because of severe hypertensive disease and marked obesity. Bleeding recurred, and in 1951 a laparotomy was done. *Final diagnosis* was myomata uteri and sarcoma of the ovary.

TABLE 3

THERAPY FOR RECURRENT BLEEDING

	Cases	*Per Cent*
None	18	5.4
Dilatation and curettage	40	
Hysterectomy for benign disease	13	16.8
Hysterectomy for malignant disease	3	
Total	74	

Discussion

Although the percentage of malignancies among postmenopausal bleeders is much lower in our present survey than in previous studies in our Department,[2-4] the incidence is still sufficiently great to make it imperative to exclude malignancy by cervical biopsy and curettage. The decrease in the incidence of malignancy percentagewise is due chiefly to the fact that the public and profession have become more alert to the possible seriousness of this symptom and more investigations are done for less conspicuous bleeding. The earlier detection of cervical cancer and the increase in estrogen therapy are also factors.

The primary purpose of this paper is to focus attention upon the benign bleeders and to determine their ultimate fate. With the increased safety of hysterectomy, both abdominal and vaginal, there appears to be a tendency in some clinics to do a hysterectomy for minor benign lesions which in a large percentage of cases can be cured by curettage alone. Judgment as to the necessity for definitive therapy for postmenopausal bleeding not associated with malignancy may be found by the answers to the questions asked at the beginning of this paper.

Question 1. How frequently does postmenopausal bleeding recur after the initial curettage fails to reveal malignancy?

There was a recurrence of bleeding in 22 per cent of our cases followed from one to eight years.

Question 2. How often is the basic and often serious pathology missed at the initial curettage?

This question can best be answered by analyzing the 3 cases in which malignancy was discovered subsequently. In case 1, there seems little doubt that the malignancy of the endometrium was missed at two curettements. In the presence of a large irregular uterine cavity associated with fibroids, this possibility always exists and should be kept in mind. Fortunately, hysterectomy was advised because of the myomata which were thought to be the cause of the bleeding. Adenoacanthoma of the endometrium was discovered and the definitive therapy was adequate.

In case 2, malignancy was discovered four and a half years after the curettage, and it

is almost certain that the adenocarcinoma was not present at the time of the initial curettage.

In case 3, the ovarian sarcoma could only have been discovered by laparotomy which would have been done immediately except for the tremendous obesity and hypertension. The diagnostic curettage cannot be judged as inadequate in this case.

Curettage, then, failed as a diagnostic study only once in 333 cases.

Question 3. In the patient with benign pathology, how often is definitive therapy ultimately required?

In the 333 benign cases which were not given definitive therapy at the time of curettage and which were followed in this report, hysterectomy was ultimately necessary in 16.

Question 4. How long should one persist in diagnostic and minor surgical procedures in the face of recurrent bleeding?

Obviously, there is no "pat" answer to this question. The answer will depend upon several factors such as the age of the patient, the physical condition of the patient, the nature of the benign lesion, and the progressiveness of the bleeding. The follow-up study of these 333 cases would indicate that little harm can result in waiting and recuretting, if necessary, rather than immediately doing major surgery for a benign lesion in the case of an elderly woman.

Summary

It is a self-evident fact that when malignancy is found to be responsible for postmenopausal bleeding immediate, appropriate, definitive therapy is indicated. When a benign lesion is found or when no lesion is found to explain the bleeding, major definitive surgery is seldom indicated immediately unless one is dealing with a submucous fibroid. When bleeding recurs it should be viewed with suspicion and reinvestigated. In our series, in only 7.2 per cent was hysterectomy ultimately necessary for benign disease and in only one case in 333 was it found that malignancy was missed in the initial curettage. An irregular cavity in a myomatous uterus was responsible for this. The small percentage of the benign cases in which hysterectomy was ultimately necessary indicates that a more hasty and radical surgical attitude would have resulted in many hysterectomies in elderly women which could have been avoided.

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The Painful Shoulder: Its Etiology, Pathology, Diagnosis and Treatment*

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In considering the lesions of the shoulder joint which may produce pain, the author emphasizes the need of a basic knowledge of embryology and anatomy, as related to the shoulder joint, for an understanding approach in diagnosis and intelligent management.

TODAY IT IS MY PLEASURE to discuss lesions producing pain in the shoulder region, which often result in stiffness of the shoulder joint. The cervical disc syndrome and diseases of bone will be excluded from this discussion. Over twenty years ago Codman[1] described the shoulder as "the forgotten joint." Following publication of his book, considerable investigation has been done regarding various lesions of the shoulder. To take but one example, there are over 160 operations for recurrent dislocations of the shoulder joint.[2] Obviously, if there are this many operations, all of them cannot be the correct one for every case. Furthermore, the underlying pathologic aspects of this condition are not completely understood. To establish a basis upon which today's discussion will rest, it is necessary to review the embryology of the development of the shoulder joint, its musculature, and its nerve and blood supply.

Morphology is that portion of science which deals with the form and structure of animals and plants. Cuvier[3] published his classic "Research on Fossil Bones" in 1812, and expressed a fundamental rule of morphology, which states that the form of a tooth implies the form of the condyle of the mandible, the shoulder blade and the hand. The joint fossa, synovia and associated ligaments arise from the embryonic tissue between the rudiments of the humerus and scapula.

Joint Fossa and Capsule. The line of attachment of the capsule separates the intra-articular from the extra-articular structures. That portion of the bone which develops adjacent to the cavity zone is covered by cartilage and protected by the capsule. When rotation and descent of the upper extremity occurs the line of capsular attachment changes so there is more on the inner aspect of the humerus than on the outer. The process of the development of the capsule and its continuity with the perichondrium, later results in the secure attachment of the labrum to the glenoid.

The Muscles. Compared to the musculature of the lower extremity, which retains a very short extent of its origin to the spine above the iliac crest, the muscles moving the upper extremity retain their primitive attachment to the whole vertebral column, the skull and the iliac crest. The various groups of muscles of the shoulder girdle develop in an orderly fashion. First, the base is made secure. Second, movement of the base is provided. Third, movements between the upper arm and the base, and, finally, movement of the more distal parts is developed. This sequence progresses from the neck outward and distally, so that the muscle groups are developed in "waves," or layers. Time will not permit discussion of the development of each individual muscle moving the shoulder joint. Suffice it to say that the muscles cannot follow a completely segmental basis, such as the nerves do.

Nerves. In consideration of the applied embryology of the nerves to the upper extremity, we must recall that muscle masses receive their nerves at an early date, and as they develop in "waves" they carry their nerves with them as they keep pace with the skeletal development. This explains the lengthy course of the nerve supply to muscles such as the trapezius and latissimus dorsi. The position and width of the limb bud, in

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relation to the spinal column, determine the amount of innervation. From the spinal cord, which is opposite the limb bud, there develops the primary, anterior division and the segmental nerves which extend toward the limb bud as a sheet of fibers. The relationship of the body segments and the nerve roots to the level of the limb bud varies in different individuals.[4]

The embryonal brachial plexus is a continuous sheet of fibers, extending distally into the limb bud, which splits into dorsal and ventral divisions when it reaches the humerus. From the ventral or anterior portion arises the musculocutaneous, the median and ulnar nerves. The dorsal segment produces the axillary and radial nerves.

Blood Supply. Although of less significance than the nerve supply, the embryologic development of the blood supply to the upper extremity is important. From the primary artery of the limb an arterial network develops which extends outward into the limb bud. Later, unnecessary communications disappear, so that usually a main vessel remains corresponding to the segment. In man, as a rule, in the arm, the vessel of the seventh or central segment of the group survives as the main vessel or subclavian artery of the developed fetus. The subclavian artery may be represented by two vessels,—one much smaller than the other and in a more superficial position. In surgical procedures in this region, as well as in cases of radiating pain, vascular anomalies should be kept in mind.

Anatomy. Today we will consider anatomy in the light of the function of the shoulder joint or so-called "applied physiological anatomy." The shoulder is a ball and socket joint, which is joined to the thoracic cage only by the clavicle for bony support. The glenoid cavity and overlying acromium have been referred to as similar to an eagle's beak which receives the head of the humerus but does not produce a well-formed socket. In order to produce enough stability and still permit a full range of motion in the shoulder joint, the rotator muscles blend with the capsule of the shoulder at their insertion and form a heavy fibrotendinous cuff. This accounts principally for the stability of the head of the humerus in its relationship to the glenoid fossa. The fibrotendinous cuff of the shoulder stretches as a loose sleeve from around the glenoid to the head of the humerus. It is attached to the anatomic neck of the humerus at the top but inferiorly it reaches a half inch beyond the articular cartilage of this bone. At the glenoid it is attached beyond the rim, particularly in front, being reflected along the bone and blending with the labrum. In a normal shoulder the capsule is securely attached to bone at all points. In some measure the capsule of the shoulder joint participates in an overwhelming number of shoulder disabilities.

About eight years ago Nicola[5] listed the most common causes of pain and stiffness in the shoulder, exclusive of bone lesions, as follows: (1) ruptures and calcium deposits in the fibrotendinous cuff; (2) lesions of the articular capsule, including ruptures of the capsule with dislocations of the head of the humerus; (3) lesions of the long head of the biceps brachii tendon; and (4) the scalenus anticus syndrome.

At that time we had little concept of the embryologic and developmental importance of lesions producing shoulder symptoms. We thought that trauma of the shoulder accounted for most of the disabilities encountered, while degenerative and altered metabolic processes accounted for the others. Realizing that variations in the anatomy of the shoulder joint might cause degenerative lesions, DePalma dissected a series of 96 cadavers, ranging in age from 14 to 86 years. He found that 24 per cent of the cuff tears were in the supraspinatus tendon and 41 per cent of the tears in the subscapularis tendon. This order of frequency of cuff tears was in almost exactly opposite proportion to that which had been formerly thought to exist. We have found the incidence of the several cuff tears to vary in different localities. DePalma[6] listed these degenerative alterations in the structures of the shoulder as follows, and related them to the age at which they were most commonly found:

(1) Alterations in the articular cartilage of the glenoid fossa were found to occur as early as the second decade and to be most destructive in the sixth decade.

(2) "Wear and tear" of the labrum glenoidale were found to start early in life and progress with each decade.

(3) Degeneration of the biceps tendon was

not noted in his series of dissections before the fifth decade (over 40 years of age).

(4) The synovial ligaments in the region of the subscapularis were found to show developmental variations and he pointed out that these might be misinterpreted as capsular tears.

(5) Degeneration of the fibrotendinous cuff of the shoulder joint first appeared in the fifth decade in his series of cadaver dissections.

With this background in mind, I would like to discuss a variety of soft tissue lesions producing pain and stiffness in the shoulder region which are divided according to Bateman[4] into three groups. *Group I*—those which produce shoulder and neck pain, *Group II*—lesions which produce shoulder pain only, and, *Group III*—lesions which produce shoulder pain with radiation to the extremity, including the hand. In reviewing these groups of lesions, each will be discussed from the standpoint of differential diagnosis and their treatment will be summarized (Tables 1, 2 and 3).

TABLE 1

GROUP I. LESIONS PRODUCING SHOULDER AND NECK PAIN

Disease	*Onset*	*Relation to Movements of Cervical Spine*	*Relation to Movements of Shoulder*	*Relation to Trauma*	*Age*
Postural disturbances	Gradual	Slight accentuation	Slight accentuation	None	Older group
Fibrositis	Gradual	Slight	Minimal effect	Often repeated minor trauma	Young or middle aged
Musculoligamentous disorders	Sudden	Pain aggravated	Minimal effect	Always associated	Younger, as a rule but any age
Scapulothoracic lesions	Gradual	Very little change	Definitely related	Often associated	Younger group; often workmen

	Localization of Tenderness
Postural disturbances	Generally no points of exquisite tenderness
Fibrositis	Definite nodules or thickened areas in muscles
Musculoligamentous disorders	Definite points in ligamentum nuchae or suspensory muscles
Scapulothoracic lesions	Medial border of scapula

TABLE 2

GROUP II. LESIONS PRODUCING LOCALIZED SHOULDER PAIN

Lesion	*Onset*	*Localized Tenderness*	*Relation to Injury*	*Age*
Bursitis (degenerative tendinitis)	Gradual to acute	Present lateral to acromion	Not prominent	Young, active adults
Rupture of cuff	Sudden	Present sometimes with palpable sulcus	Prominent	Usually workmen over 50
Bicipital lesions	Gradual	Present along bicipital groove	Repeated minor trauma	Usually over 40

	Special Tests on Movements
Bursitis (degenerative tendinitis)	Abduction limited and painful
Rupture of cuff	Cannot maintain abduction. Little pain on passive motion
Bicipital lesions	Supination against resistance of the flexed forearm produces pain.

TABLE 3

GROUP III. LESIONS PRODUCING SHOULDER PAIN WITH RADIATION

Lesion	*Location of Pain*	*Effect on Radial Pulse*	*Aggravating Position*	*Age*
Scalenus anticus	Local tenderness over scalenus	Yes	Abduction plus tension	Older adults
Postural disturbances	Usually not persistent	Yes	Sleeping with arm in abduction	Adults
Costoclavicular syndrome	No shoulder signs	Yes	Hyperextension of neck	All ages
Hyperabduction syndrome	Negative in shoulder	Yes	Hyperabduction of arms	Younger group
Shoulder-hand syndrome	Positive in shoulder and hand	No	Dependence of hand	Usually over 40

Treatment

An essential part of the therapy for shoulder lesions depends upon maintaining the functional balance of the parts involved and the prevention of complications. Expressed differently, the individual having the disease is just as important as the lesion itself.

Therapeutic tests may be applied in the differential diagnoses of some of these conditions. Injections of trigger points may confirm the diagnosis and concomitantly relieve pain and stiffness in the shoulder girdle.

Routinely we divide these lesions into those which should have, (1) conservative or office therapy, and (2) those requiring hospital or surgical treatment. Fortunately, most of these conditions can be treated conservatively. The measures used include injections of hydrocortone, good physical therapy, correction of postural faults, including bad sleeping habits, proper exercises, the elimination of heavy use of the shoulder, heat, and x-ray therapy in selected cases.

It has been our experience that balanced suspension of the involved upper extremity, with the arm abducted and the elbow flexed, not only affords rest for the musculature but lessens pain and prevents an adhesive capsulitis, later diagnosed as a "frozen shoulder." While suspension treatment is being carried out, injections of hydrocortone locally into the tendon area, plus daily physical therapy, hastens recovery from acute bursitis and/or tendinitis. Before proceeding to operative treatment, including closed manipulation of the shoulder, as well as open operations, I wish to make it understood that, in our experience, proper management of the acute stage will prevent many of these lesions from proceeding to the chronic stage.

In chronic cases where adhesive capsulitis has followed improper management, a careful closed manipulation of the shoulder to break up the fibrous bands restricting motion, should be carried out under a general anesthetic. In such a procedure, nearly full rotation is accomplished before the arm is abducted far from the side. After manipulation the vertical position of the arm can be maintained best by applying balanced suspension to the affected extremity.

Usually we have found that patients with recurrent dislocation of the shoulder have not had a proper reduction under general anesthesia, and the arm has not been fixed to the chest for a sufficient length of time for the capsule to heal. It has been my experience, and that of other surgeons with whom I have discussed this problem, that we have never seen a recurrent dislocation of the shoulder following proper early treatment of the acute dislocation. The reduction should be performed by a careful manipulation that will not produce a larger tear of the capsule of the shoulder joint. The arm should be maintained in a Velpeau dressing for a minimum period of four weeks following reduction of an acute anterior dislocation of the shoulder joint.

Hospital treatment of the other lesions of the shoulder includes absolute bed rest in the very acute state, sedation, including morphine when needed for pain, and, as mentioned before, balanced suspension of the involved extremity. Although we will not discuss cervical arthritis, I wish to point out that x-ray studies of the cervical spine are very useful and should be made in all instances of shoulder pain with radiation, especially in the differential diagnosis between this condition and the scalenus anticus syndrome. When involvement of the neck is present, head traction with a halter is indicated. In certain cases fixation of the neck in a Sayre collar, or a light padded dressing and later the use of a neck brace will afford relief.

In patients having radiating pain and particularly in those patients who have the shoulder-hand syndrome, it should be recognized that this is a reflex dystrophy involving the autonomic nervous system. Therefore, blocks of the stellate ganglion, using Novocaine or one of the longer lasting local anesthetics, should be done with the hope of improving the sympathetic disorder. Although there are no sensory disturbances in these cases, there may be a contracture of the hands and fingers which often has the appearance of a Dupuytren's contracture. The shoulder-hand syndrome may follow diseases of the heart, chest, neck or nervous system, as well as primary lesions of the shoulder. I have had a few patients who required several years of treatment to obtain a good functional result. Operations for shoulder lesions in the acute stage are seldom justified.

In some chronic cases, with persistent symp-

toms and in which calcified areas are demonstrated by x-ray examination, resection of such areas by open operation may be necessary. Similarly, if a bony spur can be shown on the medial border of the scapula in a patient with a scapulothoracic lesion, it should be excised. In chronic cases of bursitis, excision of the bursa and the calcium deposit in the supraspinatus tendon may afford permanent relief. In none of our patients has excision of the acromium been indicated under these circumstances.

In ruptures of the rotator cuff, snug repair should be accompanied by resection of the acromium. This operation should not be done in elderly, sedentary patients.

In resistive bicipital lesions the long tendon of the biceps should be reattached to the humerus and its proximal end resected. In our experience this has given earlier recovery than transfer of the long head of the biceps to the coracoid process. Remember that it is necessary to remove all of the proximal portion of the biceps tendon from its groove regardless of which procedure is carried out.

In cases that are classified in Group III, where other disease, particularly in the cervical spine, has been excluded and a diagnosis of scalenus anticus syndrome has been confirmed, division of this muscle will relieve the condition.

In resistive cases of the hyperabduction syndrome, division of the pectoralis minor at its insertion to the coracoid process has been reported to give relief.[4]

Summary

(1) Applied embryology recognizing anatomic variations has been added to the etiology as a cause of degenerative lesions of the shoulder. Injury and metabolic factors producing these changes are the other etiologic agents.

(2) Some of the degenerative lesions producing shoulder joint pain and stiffness have been related to the morphology of the shoulder.

(3) The differential diagnosis of lesions of the shoulder joint has been divided into three groups and their treatment discussed.

(4) The degenerative lesions of the shoulder described are being encountered more frequently. By classifying them in the various categories listed, it will be easier to diagnose the underlying disease and apply corrective methods of treatment. I cannot overemphasize the importance of a basic understanding of the development of the shoulder joint in comprehending proper treatment. Preventive therapy is necessary to obviate complications in this group of lesions.

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Discussion (Abstract)

Dr. Julius S. Neviaser, Washington, D. C. I am in full accord with Dr. Ewing's opinion that a proper understanding of the developmental anatomy of the shoulder and its related structures is helpful in obtaining a full evaluation of shoulder joint lesions.

I take exception to the author's term of "fibrositis" and I seriously question the existence of such an entity. I feel that this term is a catch-all phrase that is used in cases when a diagnosis is not evident. For a similar reason I avoid the use of the term "bursitis," and prefer to use the descriptive phraseology of degenerative tendinitis, thus indicating the source of the pathologic process which may be complicated by a secondary involvement of the subdeltoid bursa. It is possible that the process may eventually be complicated further by an adhesive capsulitis.

Although an adhesive capsulitis or a so-called "frozen shoulder" may follow an acute lesion of the shoulder, it usually comes on insidiously so that we may not see the patient until the motion of the shoulder is markedly restricted. The prophylactic treatment is ideal if one can institute it, but it is very evident that this is rather difficult to do at times. The treatment of an adhesive capsulitis by manipulation as suggested by Dr. Ewing is to be recommended. I still think this is a good form of treatment. However, my postoperative management is somewhat different. In preference to balanced traction I tie the arm to the head of the bed by a sling in 90 degrees of abduction and full external rotation, for a period of twenty-four hours. Following this the patient is encouraged to rotate the arm internally and externally, but is not permitted to let the arm come down lower than 90 degrees. He is persuaded to try further abduction. When he leaves the hospital instructions are given for him to sleep with his arm tied to the head of the bed for an additional period of two weeks. Our results following this procedure have been uniformly successful.

The author's statement that "we have never seen a recurrent dislocation of the shoulder following

proper early treatment of the acute dislocation" is not confirmed by my own experience. Rowe, in an excellent presentation of 500 cases given at the American Academy of Orthopedic Surgeons meeting in February, 1955, indicated that there was no lowering of the incidence of recurrent dislocation whether the patient was immobilized for three or six weeks. Long periods of immobilization did not lower the recurrence rate. It was shown that shoulders exhibiting defects in the humeral head were more prone to recurrent dislocations, and such defects were the result of the trauma associated with the initial dislocation. It does not appear reasonable then that prolonged immobilization could produce any change in the defect in the humeral head and thus lower the incidence of recurrent dislocation.

Meet Us

in

NEW ORLEANS

November 3-6, 1958

Psychiatry in the General Hospital Today*

HAROLD G. SLEEPER, M.D., *Oklahoma City, Okla.*

CARE OF THE PSYCHIATRIC PATIENT raises problems which are unique, just as care of the surgical patient creates its special problems. The general hospital of this country has accepted the challenge of furnishing diversified services in the care of medical and surgical patients and is in the process of accepting the challenge of psychiatric service. This expansion or modification of services in response to patient needs, and in light of new advances of medical knowledge is part of the American pattern of life. It reflects discontent with the limitations of the way things are done now and shows the desire for more effective and efficient action. Hospital care is not established and fixed, any more than medical knowledge is complete and closed to further addition. Hospital care is shaped by the principles and beliefs of the medical profession, and if changes in care come about, they result from expanding frontiers of medical knowledge.

The aim of psychiatric hosptial service is ultimately to help patients in achieving their maximum potential in adapting to the world in which they live, at the same time allowing them the greatest possible subjective comfort. Its immediate aim is to remedy states of disordered behavior and thinking so that the individual can assume an acceptable and effective role as a social and personal unit.

These purposes are accomplished to some degree in the treatment of every patient, regardless of the nature of his illness. Yet in some cases there is sufficient disturbance of behavior or subjective life to indicate an illness referred to as a psychiatric problem.

Recognition of psychiatric illness is increasing. It is no longer necessary to emphasize that the whole individual is more than just the sum total of all of his parts or that physical symptoms can be produced by emotional stress. The medical profession in general has come to believe that stress and situational factors are important in the evaluation of any patient. The profession has supported practical efforts in the prevention of mental illness and has made wide use of psychiatric consultation. But expansion of the use of the general hospital in dealing with the psychiatric patient is needed greatly in many sections of our country today.

This use of the general hospital may assume many forms. They range from consultation service to full open and closed services for all types of psychiatric care. In 1940, there were 4,302 general hospitals in the United States, and 4,239 of them would not permit the admission of a "nervous or mental patient" if they were aware of the nature of the illness. At that time only 63 general hospitals had any kind of provision for "nervous or mental patients," even the mildest. In 1946, there were 176 psychiatric units in general hospitals. In 1954, from the most recent figures available, there were 5,280 general hospitals with 584 admitting psychiatric patients, a total of 25,011 psychiatric beds, and 264,837 psychiatric admissions. This is quite an expansion of available services and reflects the increasing recognition that this type of service is both practical and economically sound.

Many of the existing units have been in operation for a sufficient number of years to furnish accurate data regarding organization, personnel, patient needs, costs, and revenues. Yet regional problems always determine the particular type of approach a given hospital must formulate.

It is not always practical or even desirable to have a full-time psychiatric staff in every hospital. Yet it is desirable to have a close working relationship between the psychiatrist and other physicians. It has been said that other physicians benefit by being exposed to psychiatric knowledge of problems of be-

*Read before the Section on Neurology and Psychiatry, Southern Medical Association, Fiftieth Annual Meeting, Washington, D. C., November 12-15, 1956.

havior, but I must point out that the psychiatrist also benefits by being exposed to current practices in medical and surgical management. No branch of medicine profits by isolating itself from the practical application of the other specialties.

Today it is impossible for one individual to encompass all medical knowledge, especially if he intends to put this knowledge to use in treating patients. With this realization comes the increasing need to draw on our associates for their skills and professional judgment. We need to speak the same language, and unless we function side by side, we drift into different languages, different fundamental ideas, and irreconciliable approaches.

Benjamin Fairless commented that one should not kill a flea on an elephant with an elephant gun, and it is equally unwise to exclude all psychiatric patients from general hospitals because in the past some could not be properly managed there. The hospital administration depends on the surgeon not to misuse the facilities of the hospital; the psychiatrist proves equally trustworthy if the practical limits of hospital management are defined in terms clear both to the hospital and to the psychiatrist. It is as apparent that a violent schizophrenic does not belong on an open floor as it is that a patient with gas gangrene does not belong in the nursery. Fortunately, psychiatrists see other patients than those with violent psychotic states.

A careful selection of cases and the administration of the best available therapy is necessary to general hospital care. The psychiatrist functions not merely to evaluate and diagnose; he must select the best possible approach to a given case and see to the administration of the necessary treatment.

Psychotherapy is only one tool employed by the psychiatrist. Indeed, his armamentarium is growing in a manner that almost parallels that of the internist. He now has a wide variety of medications with specific effects on portions of the nervous system. He has variety even in the ways in which electroshock therapy can be given, plus the use of insulin and other somatic therapies. Psychoanalysis remains as a long-term approach to certain conditions, but does not by any means represent the only way to deal with psychiatric illness.

Like wheels within wheels, there are now specialties within specialties. In the field of internal medicine we may have the cardiologist, the allergist, and many others. In the field of psychiatry there are those who deal primarily with psychotherapy and those who deal with somatic therapies. There are those who are concerned with institutional practice and those who prefer private hospital practice. The medical profession has adequate use for all within the scope of the functions that each may serve.

In the general hospital there is a particular place for the psychiatrist versed in the problems met there, rather than the one who wishes to transfer institutional practice into a general hospital or the one who wishes to remake the other members of the hospital staff in his own image. If a common ground for understanding can be maintained, there is no reason why the psychiatrist cannot work side by side with the general hospital staff to utilize the facilities now available.

It is quite satisfying to have an efficient psychiatric nursing staff, social service, and resident physician available in a well-organized and planned hospital unit. But this picture represents an ideal not easily attained, and even though such an organization cannot be placed in every general hospital, there is much that can be done in every setting to increase available psychiatric care. It is possible to handle certain cases in open general hospitals without an intern or resident training program, and without any special provision for these cases. Of course, there is considerably more work for the psychiatrist under these circumstances, and the care that he can furnish is limited. Whenever possible, it is desirable to have some working relationship with the nursing and resident staff.

In 1940, there was a problem of too many vacant general hospital beds, and hospital administrations were seeking help to fill them with paying patients. This situation has now changed to a shortage of beds, and all too often the expansion of a new service is neglected because it is easier to cultivate the old.

Blue Cross and Blue Shield Insurance in Oklahoma has only recently been broadened to include treatment for psychiatric illness. In Oklahoma City none of the five large general hospitals provide any special care for

private psychiatric cases. One hospital will not admit any patient with a primary psychiatric diagnosis and another requires special nurses with these patients. This situation will probably be modified in the future as more general hospital beds are constructed and as further coverage is furnished by the various hospitalization insurance plans.

Yet even in this situation selected general hospital patients can be treated so long as closed service care is available, even though it is not in the same hospital.

The newer medications such as chlorpromazine and promazine give us much more effective tools for handling disturbed patients. Chlorpromazine gives promise of furnishing an effective treatment for certain cases of schizophrenia, which may be treated in a general hospital with general nursing personnel instead of with insulin coma therapy in a highly specialized treatment setup.

Electroshock therapy can be given in a general hospital. Current technics allow its use in the patient's own room, but if many patients are receiving this treatment it is advisable to set up central treatment facilities which prove to be just as practical but much more simple than operating room facilities now present.

With the consideration of these points, it becomes apparent that the psychiatrist and the psychiatric patient have a place in the general hospital today. This place can be filled with benefit to the community and to medicine.

The patient today expects the general hospital to offer all of the medical and surgical services which he may require. It is the task of our profession to see that these services are as effective and available as it is possible to make them.

Endocrine Clinic

Such great strides have been made in the field of endocrinology and metabolism in recent years that the average physician has found it difficult to keep abreast of them. In a series of *Endocrine Clinics* an attempt will be made to show how new methods can be of value in demonstrating aberrations in endocrine function and how these aberrations may be corrected by judicious therapy.

Cushing's Syndrome Secondary to Adrenocortical Carcinoma

R. GLENN GREENE, M.D., and GRANT W. LIDDLE, M.D.,† *Nashville, Tenn.*

DURING THE PAST DECADE a number of developments have combined to increase the ease with which Cushing's syndrome can be correctly recognized and treated. The wide use of steroids and corticotropin as therapeutic agents has served to make physicians in general more keenly aware of adrenocortical disorders. The development of technics for the determination of adrenal hormones in biologic fluids has made it possible to define deviations from normal with considerable precision. And, finally, the availability of synthetic corticoids has made it possible to cure hyperadrenocorticism without incurring the formerly prohibitive risk of adrenal insufficiency.

In his classic description of the disease which bears his name, Cushing[1] emphasized the features of central adiposity, osteoporosis, amenorrhea, hypertrichosis, purplish striae, hypertension, erythremia, and weakness. Anderson and her associates[2] were among the first to present evidence showing that the probable common denominator of all cases of Cushing's syndrome was hyperactivity of the adrenal cortex. Albright[3] drew a clear distinction between the adrenal disorders characterized by virilization and "pure" Cushing's syndrome, the cardinal manifestations of which were properly ascribed to the chronic oversecretion of the adrenocortical "S" (sugar) hormone. It is now known that the "S" hormone of Albright is hydrocortisone. The excess hydrocortisone in Cushing's syndrome may be secreted by diffusely overactive adrenal glands (many of which are morphologically recognizable as hyperplastic) or, less commonly, by adrenocortical tumors, benign or malignant.

The following case of Cushing's syndrome associated with adrenocortical carcinoma is described for the purpose of illustrating methods currently available for the diagnosis and treatment of hyperadrenocorticism, emphasizing those aspects which are peculiar to adrenocortical carcinoma.

Case Presentation

The patient,* a 49 year old white woman, entered the hospital in October, 1956, complaining of a two year history of weight gain, deepening of the voice, acne, high blood pressure, "nervousness," and a sufficient increase in facial hair to require frequent shaving. Her previously regular menstrual periods had ceased in January, 1955, and frequent "hot flushes" were noted thereafter. Nine months prior to admission she had undergone radical mastectomy for adenocarcinoma of the left breast. No metastases have appeared to date, 22 months later.

Physical examination (Fig. 1) revealed the patient to have a full and ruddy face. The trunk was obese, but the extremities were slender. Acneform lesions were noted on the face and shoulders. Coarse black hair was found over the upper lip, chin, legs, and forearms. No striae were present. The voice was hoarse. Tinea versicolor was noted on the chest and back. Scalp hair was wavy. There was definite temporal recession of the hair line. Pubic hair was of masculine distribution. Blood pressure was 190/110. No abdominal or pelvic masses were palpable. The clitoris was approximately 3 times enlarged.

Laboratory data included the following: Hgb. 17

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*Referred to Vanderbilt University Hospital by Dr. James R. Dade of Hopkinsville, Ky.

FIG. 1

A B

Photographs of patient taken (A) immediately before, and (B) 8 months following removal of adrenocortical tumor.

Gm. %; hematocrit 50.2%; white blood cells 6,900 per cu. mm.; a normal differential blood count; blood eosinophils 34 per cu. mm.; serum sodium 130 mEq./l; potassium 4.3 mEq./l; CO_2 25 mEq./l; chloride 93 mEq./l; calcium 8.8 mg./100 ml.; inorganic phosphorus 2.7 mg./100 ml.; alkaline phosphatase 2.7 Bodansky units. Oral glucose tolerance test: fasting blood sugar 101, 1 hour 224, 2½ hours 116 mg. per cent. Electrocardiogram was normal except for slight depression of S-T segments and T waves in all leads. Intravenous Regitine 5 mg. failed to cause a significant fall in blood pressure, and intravenous histamine 0.025 mg. failed to induce a significant rise in blood pressure. Urinalysis was negative.

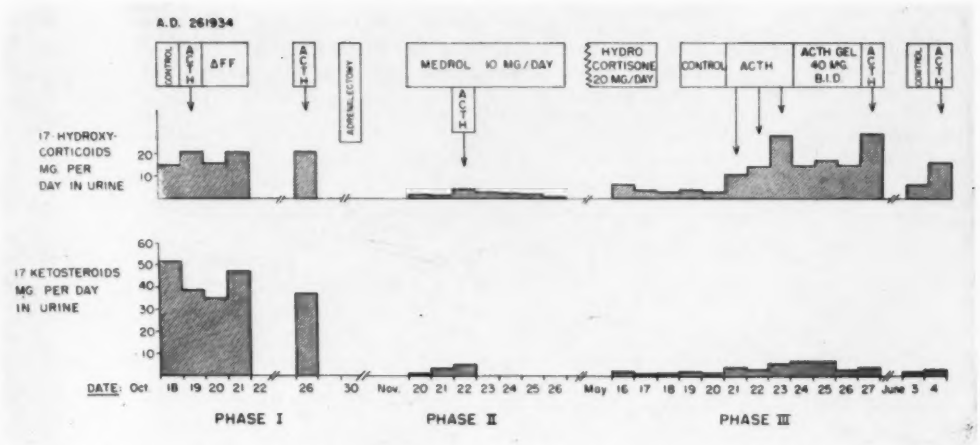
Steroid excretion data are depicted in figure 2, Phase I. The elevation of 17-hydroxycorticoids and 17-ketosteroids under "basal" conditions, the failure of these steroids to rise during treatment with corticotropin (ACTH) and their failure to fall during treatment with Δ^1-9α-fluoro-hydrocortisone are especially significant.

X-ray studies demonstrated moderate demineralization of the spine, pelvis, and ribs, and a fracture of the left 7th rib. Skull films and a gastrointestinal series were normal. Intravenous urography indicated displacement of the right kidney downward and laterally.

Operative management: With the patient under general anesthesia, the right adrenal area was exposed through a right thoracico-abdominal incision. A well-encapsulated adrenal tumor weighing 384 Gm. was removed. Regional exploration revealed no evidence of metastases. Microscopic examination of the tumor indicated it to be adrenocortical carcinoma (Fig. 3).

Medical management: Hydrocortisone sodium succinate (Solu-Cortef) 100 mg. was injected intramuscularly 2 hours before the patient was taken to the operating room. A peripheral vein was cannulated in order to avoid difficulty in providing intravenous therapy. A precipitous fall in blood pressure, when the patient was placed on the operating table, prompted the administration of norepinephrine diluted 4 mg. per liter which was given by slow intravenous infusion whenever required to prevent the systolic blood pressure from falling below 100 mm. Hg. Hydrocortisone sodium succinate 200 mg. was given as a continuous intravenous infusion during the immediate 24 hour period following the operation. Fluids infused during this period were 1,000 cc. of 5% dextrose in water and 1,000 cc. of 5% dextrose in normal saline. Thereafter, an ad libitum diet was resumed. On the first postoperative day hydrocortisone sodium succinate 50 mg. was injected intramuscularly every 6 hours. On the second postoperative day hydrocortisone 20 mg. was given orally every 6 hours. Over the ensuing week the dose of oral hydrocortisone was gradually decreased to 10 mg. twice daily. Treatment was continued at this level until May, 1957, when a course of ACTH therapy was given. Since that time no substitution therapy has been required except for occasional injections of ACTH gel to overcome the symptom of "weakness." No DOCA or other salt-retaining

FIG. 2



Daily urinary 17-hydroxycorticoids and 17-ketosteroids. Arrows represent 8 hour intravenous infusions of ACTH. *Phase I:* Note the high "basal" levels of 17-hydroxycorticoids and 17-ketosteroids and the lack of response to an ACTH infusion or to Δ^1-9α-fluoro-hydrocortisone ($\triangle$FF). *Phase II:* Following removal of the adrenal tumor the steroid levels were low and response to ACTH was negligible. *Phase III:* Following a course of treatment with ACTH gel a standard intravenous ACTH test elicited a normal response.

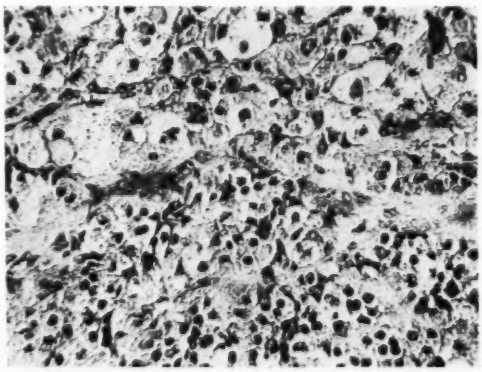
steroid was given at any time.

Postoperative studies of steroid excretion are depicted in figure 2, Phase II. During the immediate postoperative period the previously excessive urinary levels of 17-hydroxycorticoids and 17-ketosteroids were negligible, both under basal conditions and during stimulation with ACTH.

Aldosterone secretion by the left adrenal gland was apparently adequate inasmuch as the patient required neither salt nor salt-retaining steroids postoperatively. Following a deliberate course of treatment designed to deplete the patient's sodium "reserves" (low sodium diet and injection of a mercurial diuretic), the patient exhibited a normal rise in urinary aldosterone and a normal decrease in urinary sodium.

Pituitary-adrenal response to stress: In May, 1957, the patient was readmitted to the hospital for surgical exploration of a mass in the right breast and for a course of treatment with ACTH in order to restore her left adrenal gland to a normal state of responsiveness. Hydrocortisone substitution therapy was withdrawn and a standard test of adrenal responsiveness was done (Fig. 2, Phase III). Although adrenal responsiveness to ACTH was still subnormal it had, nevertheless, increased appreciably during the postoperative interval of 7 months despite the fact that the patient had been receiving hydrocortisone in doses of 10 mg. twice daily. The patient was then given a 5 day course of corticotropin gel 40 units intramuscularly every 12 hours. Repetition of the standard ACTH test at this time revealed adrenal responsiveness to be within normal range. One day following the last ACTH test a simple mastectomy was performed under general anesthesia. Neither ACTH nor steroids were administered for 16 hours before or during the operation. The procedure was tolerated well until the patient was removed to the recovery room, when her systolic blood pressure fell to 80 mm. Hg. Her circulating eosinophils at this time were found to be 118 per cu. mm., and the concentration of plasma 17-hydroxycorticoids was 31 mg. per cent. This latter value is to be contrasted with a plasma 17-hydroxycorticoid value of 45 mg. % obtained on the previous day during the third hour of an intravenous infusion of ACTH and indicates that under conditions of surgical stress the patient's pituitary failed to secrete enough ACTH to induce maximal adrenocortical activity.

FIG. 3



Photomicrograph of a section of the adrenal cortical tumor. Magnification 950 X.

Clinical course: Following removal of the adrenal tumor the patient experienced considerable loss of vigor. This has gradually improved over the subsequent year. The facial and truncal obesity have disappeared as have the acne and hirsutism. Scalp hair has increased and has lost much of its tendency to curl. Serial x-rays of the spine, pelvis, and ribs have

revealed no appreciable change in the degree of osteoporosis. The previously excessive blood pressure has consistently been found to be approximately 120/80. The glucose tolerance curve remains slightly abnormal although fasting blood sugar is now normal at 80 mg. per cent. The S-T and T wave abnormalities present in the preoperative electrocardiogram have disappeared. In July, 1957, the patient resumed regular menstruation after having had amenorrhea for 2½ years. Metastases from the adrenal tumor have not appeared.

Discussion

The most important steroid of the human adrenal cortex in facilitating the adaptation to various physiologic "stresses" is hydrocortisone. Hydrocortisone is secreted by the normal adrenal cortex only in response to stimulation by ACTH from the pituitary. Hydrocortisone in turn tends to suppress the secretion of ACTH, so that both hydrocortisone and ACTH levels normally remain within relatively narrow limits. Hydrocortisone and its major metabolites are identifiable in blood and urine by the chromogenic reaction of Porter and Silber.[4]

A number of other steroids are also secreted by the adrenal cortex in response to ACTH. These steroids have little known importance physiologically, and they have little or no ACTH-suppressing activity. Some of them are weakly androgenic. Some are chemically identifiable as 17-ketosteroids. Teleologically, it is convenient to regard them as by-products of hydrocortisone secretion.

At least one adrenal steroid, *aldosterone*, is regulated by a mechanism other than the pituitary.[5] The secretion of aldosterone is not dependent upon ACTH, and aldosterone has no significant ACTH-suppressing action. It is this steroid which is of chief importance in promoting sodium conservation and potassium excretion by the kidneys.

Cushing's syndrome may be regarded as the clinical consequence of chronic oversecretion of hydrocortisone. The chemical hallmark of Cushing's syndrome is that of excessive 17-hydroxycorticoids in plasma or urine. There may or may not be excessive levels of other steroids such as 17-ketosteroids and aldosterone. Among different patients there are impressive variations in the clinical and laboratory manifestations which have become associated with the syndrome. It is, therefore, impossible to exclude the diagnosis of hyperadrenocorticism by citing the absence of certain features of the syndrome. Patients in whom the diagnosis of Cushing's syndrome is suspected on clinical grounds are entitled to studies of plasma or urinary 17-hydroxycorticoids in an effort to establish or exclude a "chemical diagnosis" of hyperadrenocorticism.

The method of Silber and Porter gives urinary 17-hydroxycorticoid values of 4 to 10 mg. per day in normal adults. "Basal" values in excess of 12 mg. per day are characteristic of Cushing's syndrome and are almost never encountered in normal individuals. The patient described in this report exhibited levels of 15 to 28 mg. per day prior to treatment.

If the chemical diagnosis of hyperadrenocorticism is established through the demonstration of high 17-hydroxycorticoid levels, further information regarding the functional state of the adrenals can be obtained by performing a "standard ACTH stimulation test." This test is carried out by the intravenous infusion of corticotropin, 50 units, over exactly 8 hours. Most normal adults excrete from 20 to 40 mg. of 17-hydroxycorticoids during the 24 hour period corresponding to this infusion. Patients with Cushing's syndrome due to bilateral adrenocortical hyperplasia, and most of those with a benign adrenal adenoma producing Cushing's syndrome respond to this test with a marked increase in steroid excretion, generally excreting in excess of 50 mg. of 17-hydroxycorticoids on the day of the test. By way of contrast, patients with Cushing's syndrome due to adrenocortical carcinoma fail to respond with any substantial increase over their "basal" steroid output. (A single well-documented exception to this rule has been reported.)[6] Our patient was suspected preoperatively of having adrenal carcinoma on the basis of her failure to respond to ACTH.

Normally the pituitary-adrenal mechanism is easily suppressed by the administration of hydrocortisone-like steroids. For example, $\triangle^{1}$-9α-fluoro-hydrocortisone in doses of 0.5 mg. every 6 hours regularly causes a fall in 17-hydroxycorticoid excretion to about 1 mg. daily in normal individuals. In patients with Cushing's syndrome, however, the secretion of adrenal steroids is generally not suppressible by this treatment.

Since the adrenocortical carcinoma was producing such large amounts of ACTH-suppressing steroids, this patient's nontumorous

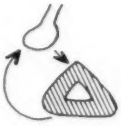
FIG. 4

Normal pituitary-adrenal relationship. ACTH from the pituitary stimulates growth of adrenal cortex and induces secretion of hydrocortisone. Hydrocortisone suppresses further secretion of ACTH.

Exogenous hydrocortisone suppresses secretion of ACTH by pituitary, permitting atrophy of adrenal cortex and cessation of hydrocortisone secretion.

Hydrocortisone from adrenal carcinoma acts like exogenous hydrocortisone. The nontumorous adrenocortical tissue undergoes atrophy and becomes unresponsive to ACTH. The carcinoma is neither dependent upon ACTH nor responsive to ACTH.

Removal of adrenal carcinoma permits pituitary to resume secretion of ACTH. The atrophic adrenocortical tissue requires time to regain its responsiveness to ACTH.



Eventually the adrenal atrophy is reversed and a normal pituitary-adrenal relationship is re-established.

adrenal tissue was atrophic and unresponsive to ACTH. The relationships between pituitary and adrenal cortex at various stages of the patient's illness are depicted diagrammatically in figure 4.

The fact that the nontumorous adrenocortical tissue was atrophic required that hydrocortisone substitution therapy be employed following removal of the tumor. On the other hand, the survival of this atrophic adrenal tissue made the long-range management of this patient simpler than that of the totally adrenalectomized individual in two important regards. First, the atrophic adrenocortical tissue retained its capacity to secrete aldosterone; therefore, neither salt nor sodium-retaining steroids were required. Second, the atrophic adrenocortical tissue under the influence of endogenous and exogenous ACTH ultimately regained its hydrocortisone secreting capacity. Barring the eventuality of metastases, therefore, the ultimate prognosis seems very favorable.

Summary

A case of Cushing's syndrome associated with a malignant adrenocortical tumor has been described. The outstanding diagnostic features were those of elevated 17-hydroxycorticoids and 17-ketosteroids which failed to increase further during administration of ACTH and which failed to decrease during administration of $\triangle^1$-9α-fluoro-hydrocortisone. Clinical and biochemical recovery ensued following surgical removal of the tumor.

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The Use of Radioactive Phosphorus and Testosterone in Metastatic Bone Lesions from Breast and Prostate*

J. R. MAXFIELD, JR., M.D., JACK G. S. MAXFIELD, M.D., and WILLIAM S. MAXFIELD, M.D.,† *Dallas, Tex.*

The extension of life in some patients having metastases to bone has been remarkable. This type of palliative treatment should be investigated further and be offered to more of these unfortunate persons.

MAMMARY CARCINOMA is one of the most frequent malignant lesions, yet it is extremely favorable to early diagnosis and amenable to adequate treatment. We believe that suitable surgical treatment plus thorough radiation therapy provides a proved method of control for the primary lesions of cancer of the breast.

Review of Literature

A review of the literature on the treatment of carcinoma of the breast shows that at the present time the greatest failing in attempts to control this malady occurs with the advanced stages of Grades III and IV and in the metastatic lesions. Such authors as Borak,[1] Garland and associates,[2] Hallberg, Nohrman and Sylven,[3] Herrmann, Adair and Woodard,[4] Leddy,[5] McWhirter,[6] Shimkin and collaborators,[7] Simmons and associates,[8] Siris and Dobson,[9] Smithers and collaborators,[10] Warren and Witham,[11] and Williams, Murley and Curwen[12] report very low five year survival figures in these stages. Many of these reported series show no five year survival of the patients treated in advanced stages of the disease.

It has long been known that relief from pain and frequently osteoplastic repair follow hormonal therapy and deep x-ray treatment directly to the metastatic lesions. The first attempts at hormonal therapy were made by Sir George Thomas Beatson[13] in 1896. This Glasgow surgeon, together with an English surgeon, Dr. H. Lett,[14] achieved considerable, though temporary, improvement by oophorectomy. By 1911, Beatson[15] was less enthusiastic and advocated operation only for those patients who had not reached the menopause and whose disease was not acute. Enthusiasm for radiation therapy as a supplement to radical surgery developed during the decade between 1910 and 1920. Oophorectomy was practically abandoned, since the majority of surgeons were unconvinced of the value of this procedure in cancer of the breast. Taylor,[16] in 1939, reviewed cases of ovarian suppression or removal and found a definite palliative effect in about one-third of the cases. Radiation was found to be of greatest use in alleviating pain caused by metastases from mammary cancer. Oophorectomy has become popular during the last few years.

Estrogens have been used with fair results in the treatment of some cases of metastases to bone, usually postmenopausal, according to the Therapeutic Trials Committee of the American Medical Association;[17-19] but Cutler and associates[20] did not obtain good results in their series of 20 cases of advanced cancer of the breast treated with estrogenic substances, showing palliative effects in only seven. Ulrich,[21] Taylor and collaborators,[22] and Huggins[23] reported relief from pain following the use of androgenic substances with a certain degree of repair in metastatic osseous lesions, but the regression was only temporary. The estrogens used by the above authors were found to be less beneficial than androgenic therapy even in patients above the 60 year age level.

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The Therapeutic Trials Committee of the American Medical Association (1949-1952) suggested that testosterone be used in cases of all ages in which the predominant lesions were in the bones. They reported results of hormonal palliation in 285 cases treated with testosterone propionate as follows. Sixty-two per cent had subjective improvement with a feeling of well-being, relief of pain, and increased physical activity. The duration of the treatment (300 mg. testosterone weekly) influenced the results since only 30 per cent obtained relief from treatment of less than one month's time. The majority of osseous lesions which regressed did not do so until after the fifth month of treatment. About 20 per cent of the patients successfully treated with testosterone were helped for as long as 9 months. On work done under the auspices of the Therapeutic Trials Committee, Van Winkle[24] reported that 77 cases of bone metastases from cancer of the breast treated for over one month by testosterone showed a 45 per cent favorable response subjectively, with only a 13 per cent objective improvement.

As affirmed by Haagensen,[25] hormone therapy should be used when surgical treatment and radiation have failed. It can add a period of palliation in a proportion of cases, even though it may not extend the length of life. Until both surgery and irradiation have been utilized to their fullest extent, hormone therapy should not be used. Once started, hormone treatment should be continued without interruption until the end, unless the patient begins to deteriorate under therapy; then withdrawal improvement may be experienced in some cases.

Elfvin[26] reported a series of cases of mammary carcinoma treated with bilateral adrenalectomy combined in the majority of cases with bilateral oophorectomy. In 44 patients in this series there were widespread skeletal metastases. Among this number, 9 deaths occurred postoperatively. Of the surviving group, 19 showed sclerosis of the metastases, with no sign of progress or spread; 8 showed progress and spread of metastases with no sign of sclerosis; the follow-up in 8 was inadequate. Relief from symptoms lasted from six months to one year in most cases, eighteen months in one case, and two years in another. The necessity to constantly control the patient by medical management, including cortisone, makes this a complicated technic. Results thus far indicate that the plan has a very limited scope.

Friedell and Storaasli[27] reported on the use of radioactive phosphorus in the treatment of metastatic osseous lesions from carcinoma of the breast. Relief from pain was excellent in this series, with occasional regeneration of the invaded bone. These authors do not advocate concurrent hormonal or glandular therapy.

We are far from a solution to the problem of mammary cancer. With some 18,000 deaths yearly in the United States from cancer of the breast, one must consider all approaches and utilize those likely to be of greatest effectiveness. Koenig and Culver[28] defined this problem by stating, "From therapy we may expect regression of the lesion itself, alleviation of the painful symptoms, improvement in the general condition and prolongation of life. This is what we mean when we speak of control of the disease process. If we can return a patient to normal life, even for a few months, we must feel that the therapy has been of definite value."

A Method of Palliative Treatment

The vast amount of material on this subject in the literature indicates the complexities of the problem and the lack of an adequate solution. More is to be desired in the treatment of the patient with metastases to bone from mammary and prostatic cancer than can be achieved by external radiation therapy, chemotherapeutic agents, castration, adrenalectomy, hypophysectomy, corticosteroid therapy, or any combination of these.

We believe our technic, documented in these pages, offers the greatest palliation possible to most patients with metastatic lesions in bone from breast and prostate. We do not propose it to be a curative procedure. Even where there has been complete destruction in certain malignant bone lesions and with the bone restored to a relatively normal structure, patients have succumbed from soft tissue metastases not affected by the testosterone-radioactive phosphorus therapy.

In our early treatment series, 1941-49,[29] we had results similar to those reported by Forssberg,[30] Friedell and Storaasli,[27] and Bell and Low-Beer[31] by the use of radioactive phos-

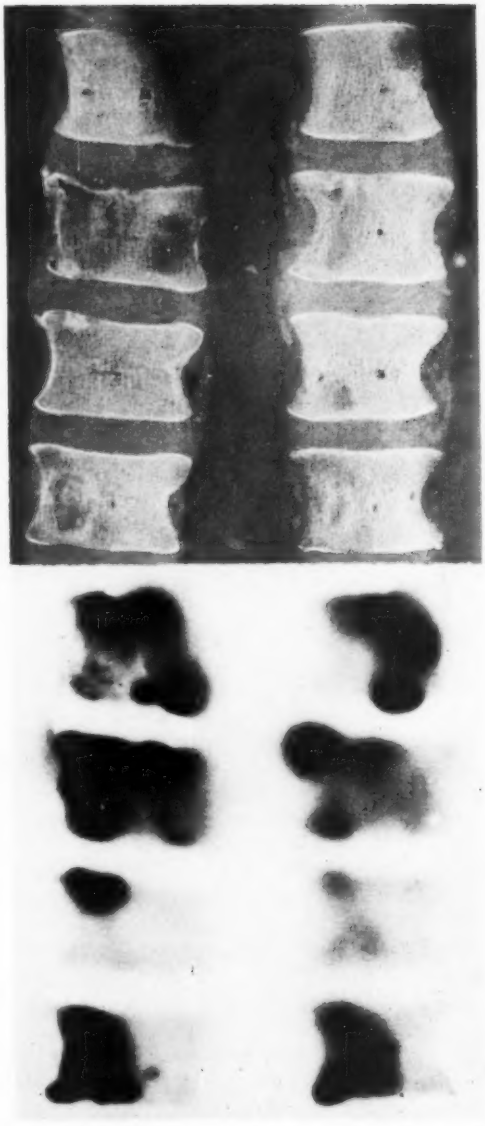
phorus in the treatment of osseous metastases from breast. We found that with smaller daily increments of P^{32} the amount absorbed in the tumor was greater and thus gave less generalized undesirable effects from the absorption of P^{32}.

We advocate the use of testosterone immediately before and during the administration of radioactive phosphorus, because it enhances the uptake of the radioactive phosphorus in the area of the metastases. It gives significantly large concentrations of P^{32} in the metastases and, therefore, allows adequate irradiation to inhibit or destroy the tumor cells. The exact mechanism of this action is not known, and investigations should be continued on this phase of the problem. We concur with Hertz[32] that possibly the testosterone causes a direct increase in the uptake of P^{32} by the tumor cell itself. Perhaps the testosterone stimulates the damaged bone in the vicinity of the metastases to lay down both calcium and phosphorus in the involved area. We do know that there is some mechanism which causes deposition of the radioactive phosphorus in significant amounts in or near the tumor cells in the bone. This has been demonstrated by scanning with a Geiger counter over areas of metastases, before and after the administration of testosterone and radioactive phosphorus and by autoradiography of bone specimens. In figure 1, the P^{32} autoradiograph shows intense uptake in the area of tumor as compared to the nontumor area. Pathologic examination of the specimen confirms the demarcation of the tumor from the nontumor area to coincide with P^{32} uptake in the autoradiograph. The differential uptake is greater than 20 times.

Having discussed the use of testosterone for the purpose of increasing the uptake of radioactive phosphorus, we will now consider the method of administration. We give 100 mg. of an aqueous suspension of testosterone, intramuscularly, daily for 5 days before the radioactive phosphorus is started and continue its use daily during the period of administration of P^{32}. On the fifth day after beginning testosterone, we give 1,500 microcuries of P^{32} intravenously. (2,000 microcuries by mouth may be substituted.)

This dose is continued daily until a total dosage of 7,500 to 20,000 microcuries have been given,—usually 12,000 to 15,000 microcuries. We try to estimate the dosage of P^{32} on the basis of the number and extent of the lesions. The largest dosage is delivered to multiple but small lesions, while the smallest dosage is given to large-size multiple lesions. The testosterone is continued for 5 days after the termination of the P^{32} therapy. Then all

FIG. 1



Note highly selective uptake of P^{32} in area of tumor, and low concentration in normal bone mass. Autoradiograph exposure 3 hours.

hormones are discontinued.

We do blood counts twice weekly during the course of this therapy and at weekly intervals for some eight weeks thereafter, as well as certain blood chemical determinations. We have seldomly had a severe hematologic problem. The patient usually requires only a supplement of liver extract with vitamin B_{12}, B-complex, and iron preparations to maintain satisfactory hemograms. We give dicalcium phosphate, B-complex, and iron preparations orally for two months following completion of this treatment.

In our series of 137 cases of metastatic bone lesions from cancer of the breast treated with the technic described, 129 had relief of pain. In the 137 cases there was good filling in of the lesions in 23, evidence of reparative effort in 41, no demonstrable change in the lesions in 26, further destruction but usually relief of pain in 47. Although this is a palliative procedure, 5 patients in this series have survived 5 years following treatment.

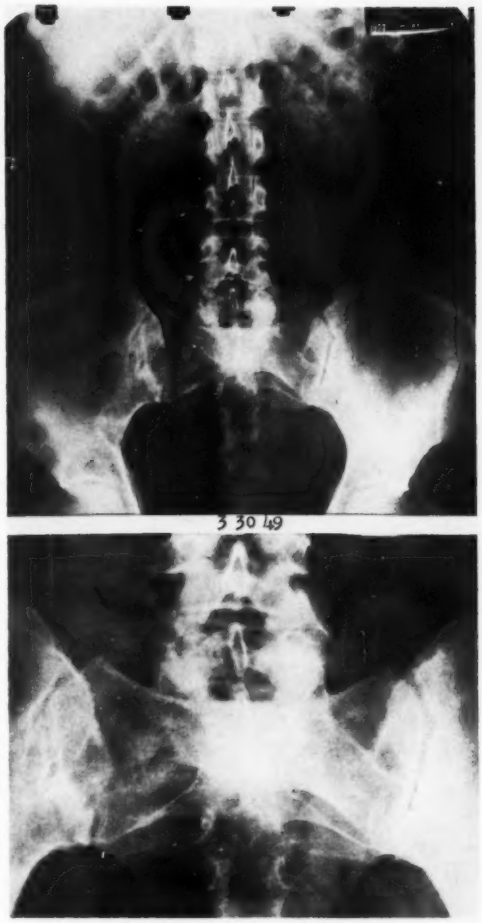
The following case summary and figures 2, 3, and 4 show the excellent response we have obtained by this method of treatment.

Case 1. E. J., a 52 year old white woman, had a mastectomy of the left breast on November 3, 1944, at the St. Francis Hospital in Wichita, Kansas. The diagnosis was solid duct cell carcinoma, grade II (scirrhous), with metastases to axillary lymph nodes. She received x-ray therapy to the breast area and back; pelvic sterilization was done in Kansas. She was free of symptoms until November, 1948, when the back pain began with increasing severity and unrelieved by aspirin.

The patient was given injections of 50 mg. of testosterone daily from November, 1948, to February, 1949, while in Oklahoma City, but the pain in back continued without improvement. When she consulted us in March, 1949, she was requiring narcotics every 4 hours, was getting progressively worse, unable to walk, and was admitted to the hospital by stretcher. On March 30, 1949, x-ray films (Fig. 2) showed breaking down in the bony structures of the pelvis, ribs, and lumbar vertebrae. From March 30 to April 24, she received a total of 2,400 mg. of testosterone (100 mg. I.M. daily) and a total of 18,500 microcuries P^{32} (1,500 microcuries I.V. daily). Her pain was relieved in two weeks after P^{32} was started. On July 5, she was free of pain and had resumed her work. She was taking vitamins and iron, eating an unrestricted diet, and needed no transfusions. X-ray films on this date (Fig. 3) showed osteoplastic filling in of the lesions, some three months after treatment with the radioactive phosphorus and testosterone.

On March 20, 1954, films (Fig. 4) show excellent healing with normal bony architecture 5 years after P^{32} and testosterone therapy. She had palliation for about 2 additional years, with no breaking down of the previously healed areas of the skeleton at any time. Several new bone lesions had occurred as well as soft tissue lesions terminally, but the cause of death was due to extensive soft tissue metastases.

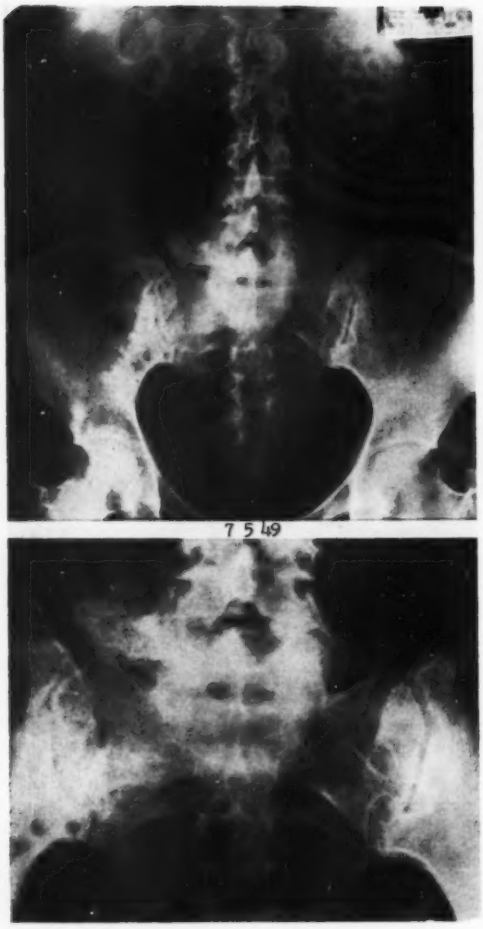
FIG. 2



These films show the destructive changes in bones of lumbar spine and pelvis. Note particularly the transverse process of the 5th lumbar on the right.

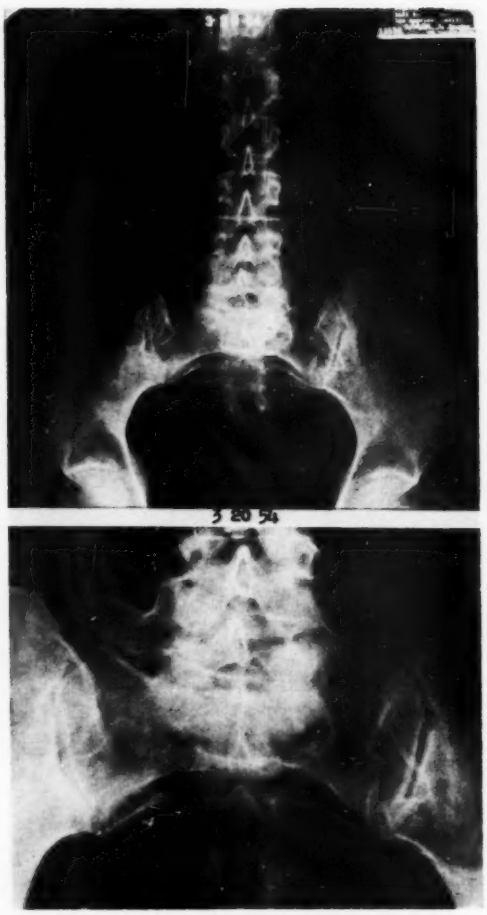
After the successful response of metastases from mammary carcinoma to bone by the use of the radioactive phosphorus-testosterone technic, we applied this method to some cases of prostatic cancer with metastases to bone. We selected those patients who were having pain, were difficult to stabilize, and were not responding to prescribed treatment. It was only after careful deliberation that we gave the testosterone. The first cases treated with the radioactive phosphorus and testosterone were those having little, if any, osteoplastic

FIG. 3



These films show the osteoplastic filling in of the lesions about 3 months after treatment with P^{32} and testosterone. Patient is free of pain and back at work.

FIG. 4



Excellent healing of involved areas of bone, 5 years after treatment with P^{32} and testosterone. Note normal appearance of the bone architecture.

phase. In some of the patients there was severe reaction during the first few days, but they later had dramatic relief by using this therapy. When these patients showed symptomatic relief and a dense filling in of bone, we began treating those who had osteoplastic metastases that were not controlled by usual modalities of therapy. Some of these men had large breasts as a result of previous intense treatment with female hormones, but still had persistent and uncontrollable pain. For these cases of osseous metastases from prostatic cancer, we used the same dosage schedule of testosterone and P^{32} as described above, except that after the last dose of testosterone the patient was put on 0.05 mg. ethinyl estradiol by mouth daily for one month. All hormones were then discontinued if the patient was symptom-free.

We have treated a series of 21 cases of metastatic bone lesions from cancer of the prostate with the above technic. This method was not successful in 5. (The patient either expired shortly after treatment or did not get relief of pain.) In the remaining 16, there was subjective improvement with definite relief of pain. Of this group of 16, there was objective improvement in the bony structures in 10 cases.

The following case summary and figures

FIG. 5

4-28-54

Multiple areas of metastatic involvement in the bones of the lumbar spine and pelvis are shown. Pain required narcotics.

FIG. 6

9-1-54

Approximately 4 months after P^{32} and testosterone treatment. Note dense osteoplastic fill in. This is particularly noted in some areas where previous films show but little evidence of involvement. Patient free of pain and working.

5, 6, and 7 illustrate the excellent response we have obtained by this method of treating metastatic bone lesions from prostatic cancer.

Case 2. R. P., a 59 year old white man, had grade III carcinoma of the prostate in September, 1953. He was treated with Au^{198} and castration with apparent control of the primary lesion. In January, 1954, he began having back pain and was put on 15 mg. diethylstilbestrol daily. During the Spring of 1954, he was having increasing pain and required narcotics.

On April 28, 1954, x-ray films (Fig. 5) showed multiple areas of metastases in the bones of the lumbar spine and pelvis. The P^{32} and testosterone technic was begun. He received a total of 13.000 microcuries of P^{32} and a total of 1,500 mg. of testosterone. His pain was definitely better seven days after the radioactive phosphorus was started, with no pain after the tenth day. He was given orally 0.05 mg. ethinyl estradiol daily for one month thereafter. All medications were then discontinued.

On September 1, 1954, x-ray films (Fig. 6) showed dense osteoplastic deposits. He had complete relief from pain, gained ten pounds in weight, needed no medications, and had resumed his work as farm mechanic.

On October 30, 1956, films (Fig. 7) showed marked clearing of the lesions. He was symptom-free and

FIG. 7

10-30-56

These films over two years later show marked clearing of the dense osteoplastic deposits. Patient symptom-free. Takes no medication. Works hard daily.

needed no medication. He had not missed a day from work since August, 1954, three months after we started his treatment. We check him periodically and will retreat him if we find evidence of metastasis again. We encourage him to live as normal a life as possible during his remission phase.

Conclusions

We feel that the advantages of our technic in using radioactive phosphorus concurrently with testosterone, to treat metastatic bone lesions from breast and prostate are that it,—

1. Eliminates prolonged use of hormones, thereby minimizing the undesirable effects of hormones.

2. Relieves pain, thereby reduces or eliminates prolonged narcotic drug therapy with resultant problems.

3. Eliminates radiation sickness.

4. Reduces the treatment time and visits of the patient to the physician.

5. Offers nominal expense to the patient.

6. Provides maximum comfort with the possibility of a spectacular reparative change in bone for long periods of time in even extensively involved areas.

7. Provides a relatively safe procedure with no more complications than found in other methods used to treat advanced malignant disease.

8. Provides a simple but effective method of treatment with much less incapacitation of the patient.

9. Offers the possibility of repetition of treatment after three months, if indicated.

Acknowledgments

We wish to express appreciation to the Schering Company, and particularly to Dr. Edward Henderson for supplying Oreton and Estinyl used in this work; the Atomic Energy Commission for their cooperation and assistance by subsidy of the radioactive phosphorus used in this investigation; Dr. John H. Lawrence and his University of California staff for supplying cyclotron produced P^{32} used in our early studies of this problem, counsel, and encouragement through the years; Dr. J. L. Goforth, our pathologist; Dr. Vincent Vermooten, our urologist; Mr. Don Kundey, our electronics technician; and our entire staff.

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Discussion (Abstract)

Dr. Robert J. Fink, Eau Claire, Wis. Since I have heard that I was going to comment on the paper by Dr. Maxfield, I have written several other investigators who are using his technic to learn what their results have been. The first paper with which I was familiar was that by Lackey, from the Presbyterian Hospital in Denver, Colorado, given before the Rocky Mountain Radiologic Society in Denver, in 1954. He stated they had begun treating cases by the technic outlined by Dr. Maxfield in January, 1954, and at the time of the meeting reported on 38 cases, all with bone metastases. These patients had all had previous courses of local x-ray treatment and hormones. The treatment as they outlined it consisted of 100 mg. of testosterone for three days, which was then continued through the course of treatment with P^{32} for three days afterwards. The P^{32} was given intravenously or by mouth in five doses over a 5 to 12 day period. The total doses ranged from 6.5 to 7.5 millicuries.

The results were as follow: In 19 cases, 50 per cent of the cases treated, there was complete relief of pain for a period of 3 to 18 months. In 9 cases, no relief was obtained. All of the patients who responded unfavorably had extensive soft tissue metastasis and died within a few days or a few weeks. They stated that they now consider extensive soft tissue metastases a contraindication to treatment. In the remaining cases moderate relief was obtained and treatment was considered worthwhile. An analysis of the cases revealed that they had pathologic fractures which would explain the persistent symptoms rather than the tumor metastasis themselves. Six of the cases which responded favorably showed evidence of healing with re-ossification in a period of 2 to 4 months. Complications occurred as two instances of aplastic anemia. One of these died and the other responded to blood transfusions, and was free from bone pain up to the time the report was issued, a period of 7 months. They reported no symptoms of gastrointestinal irritation following oral administration, and symptoms of radiation sickness were absent or slight. I have written recently to Dr. Lackey and he told me that his series now runs to a total of 52 cases. The proportion of relief and complications are the same as in the cases summarized in the paper. The same is true in the results of re-ossification of the lesions. One of their patients is improving for a period of two and one-half years following treatment and is still asymptomatic.

Another group of investigators at Harper Hospital in Detroit, includes Dr. Hayden and Dr. Corrigan, Director of the Radiology Research Department. Dr. Corrigan has written me that they had treated eleven cases by the technic outlined by Dr. Maxfield and their results are as follow: One case, they stated, was too recent to fully evaluate but has had an immediate relief of pain. Two cases responded unsatisfactorily, 8 cases had relief of pain. Of these eight, six had very satisfactory results and two had only moderate relief of symptoms. Of the two unsuccessful cases, they found on further investigation, that one of the patients had been taking premarin about which they did not know. It resulted in no demonstrable uptake of P^{32} by the tumor tissue. The other case that responded unsatisfactorily had extensive soft tissue metastases. They are continuing their work.

Our studies run only over the last year and we have treated 11 cases. In 5 cases the results have been satisfactory with relief of pain from 2 to 10 months. A sixth case had an extremely good response with relief of symptoms but has been treated only two months ago and is not adequate for evaluation. Of the 5 remaining cases, 2 died within one month and another died within six months. Two of these 3 patients had extensive soft tissue metastasis. The third has received a course of Thio-Tepa several months before the P^{32} therapy and following treatment developed a pancytopenia and expired within a few weeks. Two cases were lost to follow-up after two months but had received no relief from pain at that time.

While not a cure, the results seem to indicate that some relief of pain can be obtained by this procedure in 60 to 75% of cases.

Notice we had no selection of cases and those who responded poorly usually had extensive soft tissue metastases. It might be wise to select for this treatment those patients with predominantly bony metastasis and to consider those with extensive visceral metastasis to be poorly suited for treatment.

Dr. Maxfield (Closing). I appreciate Dr. Fink's remarks. The use of our technic by Dr. Lackey and by Drs. Hayden and Corrigan has expedited the wide acceptance it is now receiving. Let me emphasize that it is not a curative but a palliative procedure for patients with metastatic bone lesions from breast and prostate based on the phenomenon of P^{32} being deposited in the bone metastasis. Although this therapy does not usually affect soft tissue metastasis, we feel that even when there is extensive soft tissue involvement it can be used for relief of coexistent bone metastasis provided the low dosage range is followed.

Thank you for the opportunity of presenting this paper to you and for your interest in our approach to this vital problem.

Renal Infarction*§

GEORGE C. SIVAK, M.D., and ROBERT LICH, JR., M.D.,† *Louisville, Ky.*

Renal infarction is most often a complication secondary to cardiac or distant vascular disease. Thus the urologist has not had an active role in such cases. Now, however, with better technics he is called upon more often in diagnosis, and may well play an important part in saving life by early nephrectomy and occasionally by embolectomy.

RENAL INFARCTION is a disease of acute onset, manifested by severe symptomatology, and yet is rarely diagnosed either preoperatively or before postmortem examination. Although this disease can be diagnosed by the urologist with a great deal of accuracy, it is unusual for a patient to be admitted directly to the urologic service. Hoxie and Coggins,[1] in an analysis of 14,000 autopsies in their hospital, found 205 cases of major renal infarction; 90 per cent of these were admitted to the medical service and only 4 to the urologic service. This, however, is as it should be since infarction of the kidney is usually but one manifestation of a generalized disease. In only 2 patients of the 205 cases, was the diagnosis made before death.

In Hoxie and Coggins' study, renal infarction of one or both kidneys was found in the 205 cases, an incidence of 1.4 per cent. Of these patients, 76 per cent had definite cardiac lesions. In such patients peripheral embolization secondary to auricular fibrillation is a fairly common occurrence. However, 22 per cent of the renal infarctions were due to lesions of bacterial endocarditis without fibrillation (Table 1).

Classification

Renal infarction may be classified under three main categories: (1) arterial, (2) venous, and, (3) traumatic.

Arterial infarction has been diagnosed with great frequency in patients having rheumatic heart disease with auricular fibrillation. Emboli from the auricular appendage may partially or completely infarct one or both kidneys. Because of the obliquity of the left renal artery, 56 per cent of complete renal infarctions have occurred on the left side; the incidence of partial infarction would be even higher.[1-4] Septic infarction, because of its more grave significance and prognosis should be differentiated from sterile arterial infarction. The treatment of a septic infarction should be entirely different than that from a benign embolus.[3,5] Very few of the authors writing on the subject mention this differentiation in any detail, and in their advice on treatment fails to distinguish between septic and benign emboli. In septic infarction a potent bacterial focus has been placed in a devascularized organ which can only act as a culture bed for the organisms. Poor results with anti-

TABLE 1

SOURCES OF EMBOLISM OR THROMBOSIS OF THE RENAL VESSELS

	Cases
Rheumatic heart disease with	
Fibrillation and subacute bacterial endocarditis	3
Fibrillation without subacute bacterial endocarditis	27
Subacute bacterial endocarditis but no fibrillation	29
Neither fibrillation nor subacute bacterial endocarditis	1
Presence or absence of fibrillation not known	4
Coronary occlusion with mural thrombi	29
Coronary occlusion without mural thrombi	6
Sclerosis of aorta or renal arteries	24
Acute bacterial endocarditis	20
Pulmonary disease (empyema, infarcts, pneumonia)	7
Auricular fibrillation with intracardiac thrombi	7
Auricular fibrillation, no thrombi found	4
Hypertensive heart disease without auricular fibrillation	3
Intracardiac thrombi, cause not found	6
Syphilitic heart disease	1
Syphilitic aortitis with bacterial vegetations*	3
Venous thrombosis	4
Aneurysm of aorta	3
Septicemia and pyemia	3
Periarteritis nodosa	1
Not known	20

(*Taken from Hoxie and Coggins, Arch. Int. Med. 65 :87, 1940.)

*Read before the Section on Urology, Southern Medical Association, Fiftieth Annual Meeting, Washington, D. C., November 12-15, 1956.

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biotic therapy may be expected, since there is a lack of blood supply to bring adequate concentration of the antibiotics in contact with the bacteria.[5-7]

Venous infarction is of a more grave significance, and unless prompt treatment is instituted, the patient will die.[1,4,8] Venous infarction is usually secondary to venous thrombosis in other portions of the body. In children, especially in those under 3 years of age, infection of the gastrointestinal tract frequently precedes renal infarction due to venous thrombosis. Several large series of cases have been reported in which the finding of gastroenteritis has been a constant factor.[4,8] Because of this frequency one should be on the lookout for this complication in children seriously ill with gastroenteritis.

Traumatic infarction, secondary to trauma of the renal pedicle, is an often mentioned possibility, but its occurrence has rarely been reported in the literature.

Clinical Picture

The symptomatology is as follows. The patient usually has a severe pain in the flank region, constant in nature, and usually unremitting. Associated with the pain may be shock, generalized collapse, nausea and vomiting. Usually there is distention of the intestinal tract; urinary retention is frequent.

Physical examination will reveal splinting of the flank and abdomen, and diminished respiratory excursions on the affected side. Temperature elevation is usually moderate in arterial infarction, but will be more marked in septic infarcts or those from venous thrombosis.

At first the urine will be grossly clear, though usually there is microscopic hematuria. Later there may be gross hematuria. Leukocytosis occurs with a shift to the left and with white counts ranging from 20,000 to 25,000.

Diagnosis is almost a certainty when an excretory urogram reveals a failure of function in the affected kidney, and retrograde pyelography shows a normal pelvis and calyceal system without ureteral obstruction. Furthermore, there is a failure of urinary excretion and of indigo carmine dye on the affected side. While some have used aortography to demonstrate renal infarction, this should only be necessary in the most unusual cases.

Several findings help to distinguish venous thrombosis from the arterial type. In venous thrombosis the patient will be considerably more tender on the affected side, and usually there will be a growing mass which, as it increases in size, causes more pain and tenderness. The temperature will be higher, and the progression of the illness will be with a greatly increased tempo. At the time of the retrograde pyelographic examination, there will be seen some blurring of the renal pelvis, and usually dark brown or gross blood will be obtained from the affected kidney.

Treatment

Whereas, surgical intervention may be elective in arterial infarction, it is imperative in the venous type. Recovery from renal infarction of venous origin, has occurred only in patients having a nephrectomy on the affected side. (All others who were not operated upon, died from the venous infarction of the kidney.) It has been said that surgical intervention is unwise in arterial infarction, because of the possibility of the return of kidney function. Of the recorded cases in the literature, practically none of the kidneys resumed normal function and usually the result was an atrophic kidney with practically no function. In many instances, before the kidney was removed, hypertension was noted, and

FIG. 1

Infiltration of posterior base of lung on admission on May 17, 1956.

FIG. 2

IVP showing prompt excretion on the right side, none on the left (10 min. film).

continued to be present until nephrectomy was performed. Following removal of the affected kidney a return of the blood pressure to normal occurred. In all fairness it must be mentioned that the hypertension was of several weeks duration before the kidney was removed, and therefore the long-term outlook for the hypertension cannot be stated. Recently Poutasse has reported 3 cases of long-standing hypertension which were cured by unilateral nephrectomy. In septic infarction early surgery is probably always indicated.

Pathologic Changes

The pathologic anatomy of arterial infarction can easily be imagined if one visualizes a clamp placed on the renal artery. A non-functioning kidney will result and the kidney cannot increase in size. If any increase does occur it will be minimal and only through a few small vessels from the capsule or from the lymphatics. If a major portion of the arterial supply is occluded, spasm of the remaining vessels will cause ischemic necrosis in the unaffected portion of the kidney. In a few days some increase in size may occur as kidney substance breaks down and colloidal pressure increases. It has been shown in many experimental animals that occlusion of the renal artery for over one and a half hours will result in irreversible necrosis of the kidney; under one and a half hours engorgement will ensue but function will return. Undoubtedly small infarctions occur frequently, but the symptoms are mild, and may be overlooked by both, patient and physician.

Case Report

On May 16, 1956, this 31 year old white man was seen in the genitourinary clinic complaining of urinary retention and severe pain in the left costovertebral angle and left flank.

He suddenly developed this pain 2 days before. It had remained constant, was not of a cramping nature and without any radiation. Shortly after the pain developed he noticed difficulty in urination. On consulting his physician he was found to have microscopic hematuria in a voided specium. Treatment was begun with penicillin and codeine; after 2 days he was brought into the hospital because of complete retention.

The history revealed that he had been admitted to this hospital 14 days before because of pain in the right side of the chest, coughing of blood-tinged sputum, and a temperature of 103° F. At that time the x-ray and physical findings were compatible with pneumonia of the right lower lobe. He was treated with Achromycin, and in 4 days his temperature was normal, and the chest cleared. He remained in the

FIG. 3

Normal retrograde pyelogram on the left side.

FIG. 4

Gross specimen of infected kidney.

hospital for an additional week having a normal temperature. While in the hospital he was diagnosed as having rheumatic heart disease, inactive. He was discharged because of his refusal to have diagnostic studies done to evaluate his cardiac condition.

Physical examination revealed a pale white man who appeared to be acutely and chronically ill, and was in obvious distress with flank pain when lying down. There was limitation of respiratory movement on the left side. Abdominal examination revealed a distended bladder, marked tenderness in the left costovertebral angle including the entire flank region. Muscle guarding of the left anterior abdominal wall was present, as well as splinting of the left chest. Rales were heard in the left lower lung fields posteriorly; definite diastolic and presystolic murmurs were heard. The heart rate was 100, with regular rhythm, and a blood pressure of 156/100. The temperature was 103° F.

A K.U.B. x-ray film showed normal kidney shadows, without evidence of stone overlying the course of the ureters, there was some distention of the small bowel as seen in paralytic ileus.

The initial impression was infarction of the left kidney and possible pyelonephritis. Pneumonia of the left lung posteriorly was diagnosed. X-ray study of the chest showed a homogenous shadow in left posterior chest which was thought to be an infarct, or to represent atelectasis or pneumonia (Fig. 1).

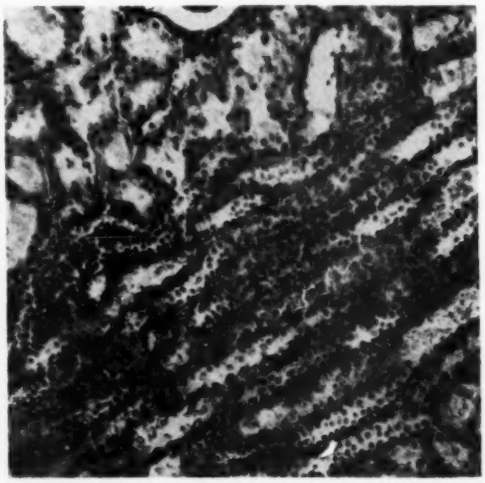
Laboratory studies revealed an N.P.N. of 28 mg. per 100 cc. The urine had a specific gravity of 1.018, a trace of albumin, no sugar, and microscopically showed numerous red and white cells and bacteria. The white blood count was 20,600 with 74% polys. The red cell count was 4.55 million, the hematocrit was 41.1% and Hgb. 12.4 Gm. After intravenous fluids the counts on the following day showed a white count of 19,400, with 76% polys., a Hgb. of 11.2 Gm. and a P.C.V. of 36.7%.

An intravenous pyelogram showed prompt excretion of the dye on the right side, none showing on the left side at the 5, 10 and 15 minute films and also at one hour. Figures 2 and 3 show a normal ureter, pelvis and calyceal system on retrograde pyelography. However, no urine or indigo carmine dye was obtained from this kidney except for 5 cc. of blood-tinged fluid in 8 hours.

Course. The temperature remained at 103° F. in spite of antibiotics. Because of the clinical course, fever and failure of improvement, it was felt that septic infarction of the kidney probably had occurred, and that exploration with possible nephrectomy were indicated.

At operation the perirenal fat was found to be markedly hemorrhagic, and condensed to a one inch layer. The kidney was normal in size and very pale in color. Pulsations could be felt distal to the renal pedicle but not at the pedicle. Gerota's fascia and the perirenal fat layer peeled off quite easily with blunt dissection after a cleavage plane was found. Between the upper and lower poles of the kidney were found definite demarcated areas of erythema surrounded by a pale border. Since it appeared that at least two-thirds of the kidney had been infarcted a nephrectomy was done (Figs. 4 and 5). After operation antibiotic therapy was continued because of the possibility of subacute bacterial endocarditis. He made an uneventful recovery from his operative procedure.

FIG. 5



Section showing tubular cell degeneration secondary to renal infarction.

Summary

A brief discussion and review of the literature of renal infarction has been presented. The different types of infarction have been discussed. The diagnosis may be made by the use of both intravenous and retrograde pyelograms, though it is seldom made preoperatively or before necropsy. A case of arterial infarction is presented to demonstrate the diagnostic points.

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Discussion (Abstract)

Dr. Hjalmar E. Carlson, Kansas City, Mo. I want to thank Drs. Sivak and Lich for giving us this excellent and comprehensive review on renal infarction. The incidence of the different types of renal infarction can be illustrated by the collected series of Regan and Crabtree who, in 1948, collected 94 clinical cases including 4 of their own, supported by urologic findings or autopsy. Of these cases, 71 were due to arterial occlusion (76%), 20 from venous occlusion (21%), and three cases (approximately 3%) were due to traumatic infarction.

The etiologic factors in arterial infarction include rheumatic heart disease, subacute bacterial endocarditis, coronary arterial disease with a mural thrombus, and sclerosis of the aorta or renal arteries. Multiple lesions in the kidneys are common. I have seen many cases of arterial infarction discussed or presented at clinical conferences. The relationship of gastrointestinal infections to the venous infarction in childhood has been stressed by the authors. It may also be associated with enteritis in the adult, with severe pyelonephritis, thrombophlebitis of the veins of the leg, puerperal infections, pneumonia, pyemia, or mesenteric thrombosis. Venous infarction is also common in kidney tumors and is largely due to the presence of tumor emboli.

In addition to an unknown number of cases of arterial infarction I can recall having operated upon a patient with a venous infarction, and one with a traumatic infarction of the kidney.

Case 1. This patient with a traumatic infarction was a soldier, 26 years of age, who had recently been evacuated by air during the Normandy invasion. He had been injured approximately three weeks previously by a wooden bullet fired from a machine gun; this had entered his spine to the right of the midline, and transected the spinal cord at about the level of the first lumbar vertebra. A laminectomy had been done and he was on suprapubic cystotomy drainage on hospital admission. Examination showed a total paraplegia.

During the second week of his hospital stay he began to pass gross and very dark blood in the urine through the cystotomy tube. This increased within two or three days, and on cystoscopic examination was found to come from the right kidney. A retrograde pyelogram was normal. There was little discomfort since he was a paraplegic. On examination no mass was palpable in the region of the right kidney, but an enlarging pulsating mass developed to the left of the midline. Blood counts showed that the red count and hemoglobin were dropping precipitously to low levels (20% Hgb.), and he was transfused. The mass increased in size, the hemoglobin continued to drop, and he was explored through a left paramedian incision. A large traumatic aneurysm of the aorta was found. He died within a few days, and at autopsy a degenerating, dark red, soft right kidney was found, completely separated from its pedicle.

Case 2. The second patient was a white woman, age 49, who was seized with a sudden severe pain in the right flank as she straightened up from baiting her hook while fishing. The pain was sufficiently severe that she was taken to a nearby hospital. She passed grossly bloody urine on her admission to the hospital; this continued for the following three days, when she was transferred to a Kansas City hospital. She gave a further history of having had a less severe episode of pain several months prior to the present attack, but this disappeared in a short time. She had also had rather severe hypertension for many years. On her admission she was found to have a large mass in the right upper quadrant, which was some 7 or 8 inches in diameter, which was tender and fixed. She was in moderate shock and was immediately transfused. The urine was dark but not grossly bloody at this time. Hemoglobin was 48 per cent. She had a slight elevation of temperature.

On cystoscopic examination a few small clots were found in the bladder. The ureters were readily catheterized and both right and left pyelograms were normal, both in anteroposterior and lateral views. Transfusions were repeated, and on the following day the right kidney was exposed. The entire kidney was found surrounded by a tremendous mass of blood and blood clots which were scooped out by the handful. The kidney was mobilized and the remaining clots and the kidney were removed.

The specimen as removed measured 18 by 15 by 7 cm. in size, and on dissection the kidney was found to be rather small and approximately 9 by 6.5 by 3.5 cm. In the middle third of the kidney was a V-shaped area consisting of a blood clot, extending down into, and apparently replacing the kidney parenchyma in this region. Close to this there was a cystic space having a thin, fibrous wall containing some bloody fluid and attached to the capsule of the kidney. In the upper pole of the kidney were three small hemorrhagic softened foci having a faintly yellowish tinge.

The largest of these was about 2 cm. in diameter. In the gross examination there was no evidence of aneurysm or any evidence suggesting tumor.

The final diagnosis was infarct of the kidney, probably of venous origin and secondary to a pyelonephritis, with a massive intrapelvic and perirenal hemorrhage. The blood pressure six months after operation was 170/110.

Dr. Charles Rieser, Atlanta, Ga. We should be grateful to Drs. Sivak and Lich for this splendid paper which has performed a great service in calling attention to the subject of renal infarction. This condition has generally been regarded as a disease for the internist since approximately 75% of the victims have associated heart disease. With the awareness that hypertension may be associated with or be caused by lesions of the kidney amenable to surgery, the internist has been requesting the assistance of the urologist more frequently. In Ormond's series of 52 cases of arterial infarction recorded in the Henry Ford Hospital, in the 20 year period between 1926 and 1946, only 10 were seen by the urologic service. The request for the help of the urologist in diagnosis, particularly in the less obvious cases, and in formulating treatment has aroused enthusiastic interest. Serious thought should be given to a revision of our thinking of causative factors, to dissemination of information as to specific criteria of diagnosis, and more particularly to flexibility of judgment in treatment.

Causative Factors. Infarction of the kidney implies a partial reduction or complete absence of blood supply in the main renal artery. This abnormality may be sudden, as in embolus originating from associated cardiac disease, or gradual in instances where heart disease is not evident. Arteriosclerotic narrowing of the orifice or any portion of the main renal artery can result in infarction. Thrombosis of the aorta at the mouth of, or within the lumen of the main renal artery can also produce this condition. Congenital lesions within the channel, or extrinsic pressure on the wall of the artery can cause infarction or hypertension or both.

Diagnosis. The symptomatology and criteria for diagnosis will vary according to the causative factors. This paper thoroughly describes the symptoms and method of diagnosis in cases of sudden sizable embolism associated with cardiac lesions. Dr. Paul White published a series in which all patients had acute or chronic heart disease and he concluded: (1) pain is more often absent than present, and in this group 65 per cent had no pain or tenderness at any time; (2) renal colic is uncommon; and (3) radiation of pain to the genitalia is very rare.

Thus between the extremes of an absence of symptoms and the typical clinical picture, all grades of manifestations may occur. At times the presenting symptom is only pain resembling an acute abdomen or appendicitis. The recent development of hypertension in one known to have been normotensive previously should alert one's thinking to the possibility of infarction. Intermittent claudication, absence or diminution of the pulse in the lower extremities, or a history of impotency suggest thrombosis in the abdominal aorta which can involve the orifices of the renal arteries.

The urine may be normal or show a few red blood cells and at times hyaline and granular casts; usually albumin is present. Not infrequently there is gross hematuria. Cystoscopy may show an absence of secretion of urine or indigo on the affected side. Due to interference with arterial blood flow, the secretion of sodium and water from the afflicted kidney is reduced. Retrograde pyelography is usually completely normal or discloses edema of the mucosa of the calyces, pelvis and ureter. Excretory urography in exceptional instances may be normal, but more commonly there is failure of secretion of the contrast media. The renal shadow in recent sudden infarction is enlarged due to edema or diminished in size in chronic infarction. When occlusion of the artery is superimposed on already diseased kidneys, the findings of urography are modified by the fundamentals of the other disease. Chronic low grade infarction is recognizable by the degree of atrophy of the calyces resulting from the set scar of the parenchyma.

The most striking feature in diagnosis of either complete or partial infarction is loss of function in the face of normal pyelography. In instances where all the usual urologic investigations prove to be normal, an arterial abnormality to one kidney remains a distinct possibility and perhaps is responsible if hypertension is present. Abdominal aortography, careful comparison of measurements of the outlines of the shadows of the kidneys, and differential quantitative estimations of sodium excretion offer assistance in decision of diagnosis.

Treatment. The literature on surgical interference for sterile arterial infarct frequently infers that operation is seldom if ever indicated. With the present trend toward conservation of renal tissue, this concept may be questioned. Blockage of the renal artery in the rat has revealed that complete recovery of function occurs after 2 hours of complete occlusion, after 3 hours restoration is partial with some degree of permanent atrophy, and after 4 hours irreversible changes occur. Embolectomy of the aorta, iliac or femoral arteries has become an accepted procedure. Why should not the embolus be removed from the renal artery? And in those instances where chronic partial occlusion of the main renal artery may be demonstrated should we not ponder over the use of arterial substitutes as employed in replacement of the aorta. In August of this year Marshall reported the case of a female with rheumatic heart disease who had a left nephrectomy due to an acute embolism. At this time the right kidney was normal in function and by pyelography. One year later she reported to the hospital 12 hours following acute colic on the right side. Immediate exploration was done. An embolus was removed from the main artery at its first branch after a Blalock clamp was placed close to the aorta. Pulsation was restored but biopsy showed the kidney to be necrotic. The patient died in anuria in 3 weeks. At necropsy the area of the embolectomy had healed. This case report is the first attempt at conservation of renal tissue by embolectomy, an operation which seems feasible. The time interval between the circulatory accident and operation must necessarily be as short as conditions permit. However, one cannot be certain that the blockage is partial or complete, and therefore, embolectomy may prove

fruitful even in instances of more than 3 hours duration.

Following infarction, wherein hypertension subsequently develops, what time interval should elapse before surgery is considered? Renal infarcts are commonly found at necropsy. Yet the majority of these persons failed to develop hypertension. The infarcted area is most often a complete scar, the remainder of the kidney is of normal architecture without ischemia. The elevation of blood pressure may return to normal in 3 to 12 weeks. The experimental evidence supports the idea that viable renal tissue in combination with ischemia is necessary for hypertension to develop. Therefore, before doing nephrectomy for relief of hypertension in the infarcted kidney, if the condition of the patient can tolerate the delay, a wait of 10 weeks would seem reasonable. The particular clinical course may require modification of decision.

I am grateful for the privilege of discussing this excellently written and beautifully presented paper. I congratulate the authors for increasing our awareness of a condition that has not adequately engaged the interest of the urologist in the past.

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Radiation Therapy in Children: For Benign Conditions of the Upper Respiratory Tract*

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The authors feel there are selected cases in which irradiation therapy is indicated. They weigh the hazards of genetic and personal damage by the x-ray.

SCIENTISTS LIKE TO PICTURE THEMSELVES as devotees of the scientific method, swayed only by facts and only to the degree that the facts justify conclusions. Unfortunately, for this self-conceived image, scientists are human, possessing just as many suspicions, prejudices, jealousies, and fixed ideas as other humans. As a result every addition to our knowledge whose acceptance requires a revision of thinking, is met with either unreasonable doubt or unreasoning overenthusiasm, and emotional outbursts from those whose habits of thinking or way of earning a living must be readjusted.

Some months before daring to report his observations on the protection against smallpox afforded by inoculation of human beings with matter from the lesions of cowpox, Edward Jenner wrote his friend Gardner to describe his findings, and to beg the protection of secrecy. "I have entrusted a most important matter to you—and should not wish that what I have stated be brought into conversation; but should anything untoward turn up in my experiments, I should be made, particularly by my medical brothers, the subject of ridicule." Finally, he steeled his nerve to make a statement to the medical world in 1788. This, oddly enough, attracted little attention, but when in 1796, he published his well-known treatise, "An Inquiry Into the Cause and Effects of the Variolae Vaccinae, a Disease Discovered in Some of the Western Counties of England, Particularly Gloucestershire, and Known by the Name of Cowpox," the storm broke over his head. He had to face, not only the jeers of laymen, but misstatements, misrepresentations, and abuse from a large percentage of the medical profession. It is good to note that he lived to see the practice of vaccination adopted all over the world.

Charles R. Darwin published "The Origin of Species by Means of Natural Selection" in 1859. During his lifetime, this shy, introspective man endured fearful blasts from even such mental giants as Gladstone, Balfour, Kingsley, Butler, Arnold and Carlyle; and posthumously, as recently as 1925, at Dayton, Tennessee, he was assaulted along with biology teacher John T. Scopes by no less a figure than William Jennings Bryan.

Today we are treated almost daily to an emotional extravaganza upon the relationship or lack of relationship, between cigarette smoking and lung cancer. Obviously more than a desire for the truth is involved. Crusading zeal, the need to exonerate a deeply ingrained habit, and economic considerations are all too evident.

Around the subject under consideration in this paper, there also revolve emotion-inspired misrepresentations. Between the illogical thinker who loudly condemns the use of ionizing energy in the therapy of benign conditions under any circumstances, and the prejudiced scientists who unreasonably minimize the hazards involved, the detached physician is hardpressed to find his way.

It was at about the time of the Scopes trial, in 1925, that radiation came into general use as an adjunct in the treatment of bacterial infections. It was found that small doses, of the order of 50 to 125 r per exposure, did no recognizable injury to the infected tissue, but did break down the extremely sensitive

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leukocytes which were highly concentrated in and about the infected area. The release of antitoxins by the disintegrating white blood corpuscles and the inpouring of fresh leukocytes and macrophages strengthened the natural defense mechanism. From about 1925 until 1944, radiation unquestionably was successfully used to stimulate the body to abort many infections. It sometimes made the difference between life and death.

In the upper respiratory tract of children it was widely used to combat sinusitis, pharyngitis, lymphoid folliculitis, tonsillitis, inflammation of the eustachian tube, otitis, mastoiditis, and tracheobronchitis. In addition, it was used to shrink exuberant adenoid and lymphoid tissue and enlarged thymus glands. These tissues, made up of cells normally very sensitive to radiation injury, were even more sensitive in their hyperplastic state and were readily subdued by small doses of radiation.

In 1929, before the treatment of infections by radiation had reached its height, Sir Alexander Fleming noted that the growth of the mold *Penicillium notatum Westling* was accompanied by the release of a substance bacteriostatic and bactericidal to gram-positive organisms. However, it was not until 1944 that penicillin was produced on a large enough scale to replace older less effective methods. Penicillin, and the host of antibiotics that have followed, have made the radiation treatment of acute infections in the upper respiratory tract of children a matter of historical interest only. However, in chronic infection of this area which antibiotics fail to control, radiation still serves a useful purpose. Because bacteria unfortunately are learning to live with our antibiotics, we still have to contend with some of these chronic conditions. Since radiation does not act directly upon the bacteria but merely aids the natural defense mechanism, tolerance to it cannot be developed. Because chronic mastoiditis, tonsillitis and adenoiditis are usually terminated surgically, our attention can be turned almost exclusively to chronic lymphoid folliculitis and hyperplasia, and chronic sinusitis.

Radiation Hazards to the Individual

At this point we are confronted by the 1955 report of Clark[1] presenting the case histories of 13 children with carcinoma of the thyroid who, prior to the establishment of the diagnosis, had received x-ray therapy to the neck or upper chest. Five were treated for enlarged tonsils, 3 for an enlarged thymus, 3 for cervical adenitis, one for peribronchitis, and one for pertussis. Clark's assumption, that a relationship exists between the radiation and the carcinoma, is strengthened by the 1950 report of Duffy and Fitzgerald,[2] who noted that in their series of 28 children with carcinoma of the thyroid, 10 had had irradiation of the thymus in infancy. Simpson and his co-workers,[3] in 1955, reported that, in a follow-up study of 1,400 children who received radiation therapy for enlarged thymus in infancy, 17 developed malignancies, of which 6 were carcinoma of the thyroid. This was a significantly higher incidence than was found in their untreated siblings. Majarakis and his associates,[4] in 1956, reported that of 10 children seen by them, aged 15 and under, with carcinoma of the thyroid, all had received radiation to the head and neck during infancy or early childhood. On the other hand, Uhlmann,[5] of the Michael Reese Hospital, in 1956, published a comprehensive review of this subject and came to the conclusion that carcinoma of the thyroid in children is a neoplasm whose incidence is currently increasing, and that a statistical correlation between irradiation and the development of the disease cannot be drawn. The story is not yet complete; we do not know just where we stand but we are disturbed.

We recall the study of Warren,[6] supporting previously accumulated data indicating that radiation accelerates the aging process. He noted that, in addition to an incidence rate for leukemia of about eight times that of the general population, physicians exposed to large amounts of radiation die at a significantly earlier age than do other physicians from a variety of neoplasms, of degenerative diseases such as coronary disease, myocarditis, cerebral hemorrhage, and nephritis, and even of infectious diseases, such as bronchopneumonia and tuberculosis.

We also recall Brown's[7] review of the incidence of leukemia in patients receiving radiation for ankylosing spondylitis, in which he concluded that as little as 94 r to the spinal marrow doubled the incidence rate for leukemia. This, added to other studies of the effect of radiation upon the incidence of leukemia, increases our indecision.

What conclusion can we reach, what action should we take?

Whenever we have a patient who might be benefited by a procedure involving risk, we face the same problem and must arrive at the answer in the same way. We must first exhaust methods of treatment which do not involve risk or which involve less risk. If the patient's disease persists, we must then decide which carries the greater risks, continuation of the disease or the treatment under consideration. When we see a patient with acute appendicitis, we decide that the risk of allowing the disease to continue its course is greater than the risk of operation, though we recognize that postoperative thrombosis and embolus may occur, that postoperative pneumonia may develop, and that anesthetic deaths are not entirely avoidable.

Chronic Sinusitis

What about the child having chronic sinusitis which has not been controlled with persistent treatment, including antibiotics? The child is in danger of deafness, asthma, and bronchiectasis. He may already have developed one or more of these complications. Should he have radiation? The answer lies in the answer to these questions,—which is more apt to shorten his life, asthma or a small amount of radiation to the sinuses? Does he stand in greater peril from bronchiectasis or from radiation-induced leukemia or carcinoma of the thyroid? Because our knowledge is still incomplete, each of us must answer these questions for himself on the basis of what is available. We elect to radiate these children, but we do it carefully, making an earnest attempt to minimize possible hazards.

We use an x-ray beam of medium quality, half value layer of about 4 mm. Al, to insure a reasonable depth dose at the level of the posterior limits of the antra but a smaller depth dose at lower levels.

In consultation with the otorhinolaryngologist and with the help of the roentgenograms, we decide whether the antra alone need therapy or whether the ethmoid sinuses should be included. If the antra seem to be the major source of difficulty, we use a round cone large enough to cover the antrum comfortably, but no larger. Sometimes this portal may be only 2 cm. in diameter. Further, to insure protection of the adjoining structures, we expose the skin over the antrum through a cutout in a piece of lead or lead-rubber which is large enough to cover the rest of the face. We then give 50 to 100 r in air to first one antrum and then to the other, two or three times a week for a total air dosage of 200 to 600 r to each antrum. The exact dosage, number, and frequency of treatment are varied with the patient's age and response.

If it is decided that the ethmoid sinuses need treatment also, the face is shielded with lead or lead-rubber so as to expose the antra and the bridge of the nose. Particular care is taken to protect the eyes and brows. Then the antra and ethmoid sinuses are exposed simultaneously. The dosage and schedule are the same as when the antra only are treated.

The benefit derived from this therapy is twofold. The body's natural defense mechanism against infection is bolstered by the local breakdown of leukocytes, release of antitoxins, and the inpouring of fresh leukocytes and macrophages. The swollen hyperplastic sinus membranes are thinned, permitting better drainage of the antral cavities.

Sometimes a radiologist is consulted as to the advisability of repeating this therapy for recurrence of the sinusitis. When the patient has responded well to an initial course of therapy and the interval since therapy is at least three months, preferably six, we will use radiation a second time. In several patients, we have even repeated it a third time, but in general, repeated recurrence simply proves that radiation cannot make a contribution great enough to justify the hazard its repeated use incurs.

We believe that we have not increased the patient's hazard of thyroid carcinoma, because with shielding and limited portals, no measurable radiation reaches the thyroid. We believe that the threat from the increased hazard of leukemia and accelerated aging resulting from this dosage to a small block of tissue is less than the threat from persistence of the chronic sinusitis.

The results are difficult to evaluate. We have attempted no statistical analysis of our patients because we feel this aspect of the problem has been thoroughly analyzed.[8-10]

Chronic Lymphoid Folliculitis and Hyperplasia

Chronic lymphoid folliculitis and hyperplasia carries with it the same threat as chronic

sinusitis. The local application of radium is usually preferred for follicles obstructing the eustachian tube orifices. When the hyperplasia and infection is diffuse throughout the pharynx, the advisability of irradiation by x-ray through external portals must be considered. We will undertake the procedure if the otorhinolaryngologist has exhausted the other resources and the child's general condition is jeopardized. Again we use a beam of medium quality, half value layer of 4 to 8 mm. Al, depending on the thickness of the child's neck and face, and deliver the radiation through opposing lateral portals just large enough to cover the pharynx. We shield the thyroid fully and give 50 to 150 r in air, sometimes to both portals at one sitting, sometimes to only one, waiting 24 to 48 hours to treat the other side. We repeat this therapy at intervals of one to three weeks for a total dose measured in air of from 150 r to each side of the neck to 900 r to each side. The dosage per treatment, the interval between treatments, and the total dosage are individualized to suit the patient and his response.

Again there is a twofold benefit. The effectiveness of the body's defense against the local infection is increased, and the hyperplastic tissue is reduced. Again we feel that the chance of producing radiation injury is less than the chance that the persistent lymphoid hyperplasia and infection will produce injury.

It is not beyond the realm of possibility that the drug-resistance problem will lead to a renewed need for the help of radiation in subacute infections, even acute infections, in the upper respiratory tracts of children. Should events take that unhappy turn, we should be guided by the same principles as those we have outlined.

Genetic Hazard

A comment should be made about the genetic hazard of radiation for the conditions under discussion.

Muller, of the University of Indiana, received the Nobel prize in Physiology and Medicine, in 1946, for his discovery of the production of mutations by x-rays, a discovery which came as the result of years of work initiated in 1926. It is perfectly clear that the vast majority of mutations are undesirable. The geneticists are now able to define the danger to the race of radiation-induced mutations with sufficient exactness to lead the National Academy of Sciences to recommend that a real effort be made to hold the radiation received by the gonads in the first thirty years of life to 10 r. When we consider that the gonads receive 3 to 5 r from cosmic radiation in 30 years, the recommendation is seen to be a difficult one to follow. If radiation of the sinuses and pharynges of children involves risk of an increased rate of mutation, we should limit its use much more strictly than we do. But in addition to the protection we have already described, we place a lead-rubber apron over the patient's trunk. Since, with the protection described, the dosage at the gonads is too minute to measure, the apron is probably unnecessary. However, it makes everyone feel better, and we are certain that we are not running any genetic hazard.

Summary

The use of ionizing energy to treat benign conditions in the upper respiratory tracts of children is needed today only in stubborn cases of chronic sinusitis and chronic lymphoid hyperplasia and folliculitis.

If other measures fail to relieve the child and he develops, or is in danger of, deafness, asthma, or bronchiectasis, radiation therapy should be considered. Properly used, it involves no genetic hazard and a personal hazard more acceptable than the complications that would follow the persistence of the disease.

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Some Immunologic Aspects of Fungous Diseases*

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The author uses the fungous diseases as a basis for speculations in the field of immunology.

THE SUBJECT OF IMMUNOLOGY as it applies to the diseases caused by fungi must at first glance appear to be of little importance. I have long believed that the reverse is true; at first undoubtedly because of my own chauvinistic attitude toward medical mycology, but more recently because of the accumulation of what appear to me to be convincing facts. Much of this information is already widely known, in fact I have very little to present here which is really new, and nothing which is startling. However, I believe that by emphasizing certain facts in a particular order, the importance of mycologic immunology will become apparent to all.

It must be admitted at the outset that a full understanding of this subject would not save many lives directly, nor relieve any large number of persons of diseases which, as Rothman has so vividly expressed it, "do not destroy life, but only ruin it." While it is true that there are several fungous infections which can be fatal, such deaths are rare, totaling perhaps not more than two hundred annually throughout the world. Conversely there are fungous diseases which are extremely common but seldom deserve to be classed as more than nuisances. The importance of such studies stems from the fact that immunologic phenomena appear to follow a much simpler pattern in fungous diseases, particularly certain ones, than in other microbiologic infections. Hence it seems likely that an exhaustive study of selected mycoses could blaze pathways by which the immunology of more complicated diseases would be much more easily and rapidly clarified.

That this would be of the greatest importance may be realized by recalling that in spite of a tremendous effort, involving much complicated investigation, the processes by which animals resist many of the severe microbial infections are as yet but poorly understood. These processes include those possessed naturally as well as those which can be specifically acquired. In general, immunologic victories have been few, and some have been fortuitous. Some depend on combating a toxin; most of the rest provide a means by which a normal animal may be stimulated to develop a specific immunologic resistance against a certain subsequent infection. No impressively successful method has yet been developed by which an animal may be stimulated to develop specific resistance against an infection already present, and very little by which the nonspecific or natural mechanisms of resistance can then be enhanced. It is clear that immunology is an extremely complicated subject and to a large degree baffling to even the most astute thinkers. And certainly it is to me, due either to an inherent lack of capacity to understand it, or to some gap in my medical education. This indicates conclusively that I do not claim to be an immunologist though I speak on the subject at times.

Some may ask why it is necessary to understand immunology any better than we do at present. It will be pointed out that the sulfonamides and antibiotics have given us control of many infectious diseases, and that more such substances are being discovered each year, presenting an ever widening spectrum. Is it too much then to hope that effective medicinal antimicrobial remedies for all infectious diseases will be eventually discovered? There are several reasons why I believe this dream will not become a reality.

First it is most important to emphasize that

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benefits such as those due to antibiotics are almost certainly only of transient nature. Victories in medical therapy fall into two great classes,—those in which the agents remain persistently and equally as effective as at the time of their discovery, and those in which they do not. Examples may be cited from the major contributions of this century,—insulin is equally as effective today in diabetes as it was in 1922, and liver extractives are just as valuable in pernicious anemia as in 1929. By contrast, penicillin is at present not more than half as efficient as it was at the time of its discovery, and this change has occurred in a comparatively short span of years. Other antibiotics are similarly decreasing in efficiency as their use continues. The difference lies, of course, in the fact that diabetes and pernicious anemia are caused by inanimate chemical mechanisms and not by living microbial enemies which can by mutation "learn to fight back." Many of the causative organisms of serious diseases have already produced strains more or less completely resistant to chemotherapy or antibiotics; it would be hazardous to assume that the rest cannot do as well if given time.

As an example, in the dermatologic field, within the last year I have seen three cases of severe, extensive, deep pyoderma of the acne conglobata type, and two of carbuncles, as well as several infections involving the palms or soles, in which the causative bacteria have proved to be resistant to all common antibiotics except chloramphenicol (Chloromycetin) and novobiocin. I was impressed with their resemblance to the terrible infections we encountered in the years before the advent of the sulfonamides, and I shuddered at the realization that that era could return, after a couple of decades of freedom.

At first I took some comfort from the fact that two antibiotics were still effective, until I realized that there was a disquieting reason for this fact. With regard to chloramphenicol it seems likely that these bacteria have not yet learned how to resist it, simply because they have not yet encountered it very much. Although it is not a new drug, it has been used comparatively little because very early in its career it was discovered to be more toxic than other substances which were equally effective at that time. In the case of novobiocin the explanation probably lies in the fact that it also has only recently been used extensively. To those who may believe that new antibiotics will be discovered as rapidly as they are needed to keep ahead of our bacterial enemies, and who point to novobiocin as an example for use in my cited cases, I must remind them that this substance is not new at all, having been discovered more than ten years ago,[1,2] and bypassed in favor of others known to be more efficient and less toxic at that time. The situation parallels that of Chloromycetin, except that the latter is known to all as an old drug and as a toxic one. Novobiocin is also old, and I believe its toxic disadvantages will soon become known to all when it has been as widely used for a while. Severe reactions including one death have already been reported.[3-5] After a period of exposure the bacteria will probably learn to resist it also.

It would require only a little perspicacity to conclude that chloramphenicol and novobiocin should rigidly be held in reserve, and be used only to combat infections caused by organisms already resistant to other more commonly used antibiotics, not only because these drugs are relatively unsafe, but also because the bacteria will learn to resist them also, if they meet them often enough. Also, when they are used they should be used in sufficiently heavy dosage to be lethal to the organisms, if possible, and not in small amounts which may allow the formation of resistant mutations. At the University of California Hospital in San Francisco such restriction has been practiced, and it has been concluded that the development of resistant strains has been significantly retarded. To use a military analogy, we should keep a few tremendously potent weapons under a dense cloak of secrecy until a real emergency arises. Instead, however, these substances are now being furnished as a small percentage in combination with the more common antibiotics to "broaden the spectrum," so that lazy doctors will not need to use any diagnostic acumen whatsoever, but simply treat all infectious illnesses with the same curative "shotgun" capsule. It depresses me to realize that there is so much money to be made from these pills, that one cannot expect the pharmaceutical industry to refrain from thus selling the secrets of our medicomilitary weapons to the enemy; I do not hesitate to state

strongly my belief that such action is the analogue of military treason, which will in the future confer upon many human beings a death much more appropriately deserved by the traitors. The physicians who use such substances are even more culpable.

Furthermore, I believe there is a limit to the number and variety of different antibiotics which nature will furnish us. Most of them have come from actinomycetes found in soil, where I believe the "bottom of the barrel" has already been reached. From only a moderate acquaintance with the extent of investigations carried out by research institutions and the pharmaceutical industry, I would estimate that at least a million samples of soil have been culturally assayed in search of antibiotics. These have come from all parts of the world and from all conceivable sources,—as the dredgings from the bottom of the Mindinao Deep, the crags of the Himalayas and the inside of a dinosaur's egg. During these studies the antibiotics we use today were rediscovered hundreds of times from new source organisms, while really new ones have been less and less frequently found. It is true that a large number of such substances have been accumulated, from which we may make further selections, but many of them possess serious disadvantages; the best ones were selected early and have been extensively used ever since. As Rich[6] so aptly said "In the attainment of her ends, Nature is often profligate with materials, but she is usually singularly conservative with methods." It would seem that antibiotics are some of Nature's fundamental mechanisms, and we are likely to find that instead of bothering to think up new ones, she makes use of each such mechanism over and over again, in the same way that she employs chlorophyll or hemoglobin in a huge number of different forms of life.

I have been told that the chemists will be able to alter these antibiotic molecules so the bacteria will be kept confused. I must admit that this is possible, but I suspect there will be many disappointments also along this road. Small changes in the molecules, such as the addition of a methyl group here, a hydroxyl group there, chlorination or the like, will probably not succeed in broadening the spectrum. As an example, consider the drugs first known by their proprietary names Aureomycin and Terramycin, which were thought to be different for a long time, but finally were discovered to be respectively chloro- and hydroxyl derivatives of the same tetracycline nucleus; after a still longer time it became clear that the antibacterial spectrum of all three modifications were the same. Also, as soon as a species of bacteria was found to have developed a strain resistant to one of these, it was found also to be resistant to the others. The majority of new antibiotics announced at the "Soviet All Union Conference" on antibiotics this year were relatively simple chemical modifications of penicillin, neomycin and chloramphenicol. More fundamental alterations in the molecules necessary to take in resistant strains are more likely to destroy all antimicrobial activity than to enhance it or change its specific spectrum. There are, of course, other possibilities, such as one suggested recently to me by Dr. William S. Stone, Dean of the University of Maryland School of Medicine; this is a sort of "setting a thief to catch a thief" mechanism, wherein resistant strains of pathogenic bacteria would be grown in combination with organisms capable of producing antibiotics against the preceding nonresistant strains, in the expectation that the antibiotics thus produced might be appropriately changed also by a corresponding mutational process.

In spite of such hopeful pathways, it seems all too likely that we will eventually be confronted with infections of the usual types, but they will be due to strains of organisms which have developed complete resistance to all of our "miracle drugs." The antibiotic era will then be seen in retrospect as a wonderfully fortuitous, but temporary, "breathing spell," during which, instead of being ever more complacent, efforts should have been redoubled in a search for methods of enhancing the ability of the animal body to fight infections by those immunologic mechanisms which it naturally possesses, as well as those which it can acquire specifically.

Having thus digressed in an attempt to justify the urgency of immunologic research in general, I will now return to its mycologic aspects. Until recent decades it was accepted, apparently without argument, that the reason certain systemic fungous infections caused death so rarely was that man had contact with the causative organisms infrequently.

Now it has become evident that this is not the explanation; rather, that huge numbers of persons acquire such infections, but resist them so superbly that they either remain subclinical throughout their course, or are so mild as to attract little attention, becoming easily cured and resulting subsequently in permanent specific immunity. Admittedly there are microbial diseases, other than those caused by fungi, which behave similarly, but there are no better examples of the ability of human beings to resist potentially lethal organisms almost perfectly than is seen in coccidioidomycosis and histoplasmosis, in which probably not more than one person succumbs out of several thousand who are originally infected. To study the excellent immunologic mechanisms in such infections would therefore seem to be much more promising than in those resisted less well.

However, the above facts can be interpreted in another way which has been insufficiently emphasized heretofore. If only one of several thousand persons acquiring an infection succumbs, the fault probably is that the individual possesses an immunologic system which is deficient in some vital capacity possessed by all who are normal. This seems much more logical than that an exceptionally virulent strain of the microbe must have been encountered, or its quantity greatly increased. Either of these might be expected to occur with greater frequency than is the case in the fatal type of coccidioidomycosis or histoplasmosis. For the former we have no clue other than that persons having deeply pigmented skins resist the infection less well, particularly Filipinos. In histoplasmosis there is a potentially more significant clue in the fact that in a statistically significant percentage, the fatal form occurs in conjunction with a diseased reticuloendothelial system. It seems logical to suspect that the lack of resistance may be the result of the failure of this diseased system to perform one of its important duties, the production of specific antibodies against the causative organisms. While confirmation of this might not help us much in curing this disorder, since we would still need to await the discovery of a cure for Hodgkin's disease or leukemia, it would add much to our understanding.

I have long advocated that coccidioidomycosis should be studied immunologically with the utmost intensity, far beyond what its toll in fatalities would seem to warrant, when compared with tuberculosis for example. Here is a disease which is as protean as tuberculosis in its manifestations, and bears striking resemblances to it in most of its phases, yet behaves immunologically in a manner which seems to be much more simple. It offers an antigen capable of giving several clear-cut reactions:—one an intracutaneous response of the delayed tuberculin type which seems to parallel very closely and even quantitatively the patient's ability to resist the disease; another a precipitin reaction which indicates the presence of the disease in an active and early form; and a complement fixation capable of being quantitated throughout a wide range and whose titer seems to parallel the amount of specifically diseased tissue present at the time. The interplay of these tests serves the clinician better in determining the prognosis in a case than all other laboratory or clinical examinations combined. While there is no proof as yet that the antibody revealed by the skin test is identical with, or even related to the factor responsible for conferring specific immunity, neither is there conclusive evidence that it is not. This antibody cannot be transferred with serum or blood. Frequent multiple small transfusions of whole blood have been observed, however, to be of some apparent benefit often enough to cause speculation that some other specific antibodies may have been thus transferred. Especially is this likely when it is recalled that in certain endemic areas, an overwhelming percentage of the general population, from which such donors are drawn, are specifically immune to coccidioidomycosis, having had the disease in its extremely mild form which confers such resistance. With all of the modern knowledge of protein chemistry, electrophoresis and ultracentrifugation, discovering the secrets of such a mechanism does not appear as formidable as many another research project which has borne fruit.

Histoplasmosis also offers a similarly encouraging field for study. Many of its manifestations are very similar to those of coccidioidomycosis, which is astonishing in view of the fact that its causative organism differs profoundly, particularly by preferring to be an intracellular parasite. In addition to the apparent causative relationship with

lymphoblastomatous disorders previously alluded to, it presents other valuable clues, particularly that the very young and the very old are much more susceptible. The other deep mycoses present equally interesting clinical clues. In crytococcosis the same statistical relationship with lymphoblastomatous disease exists as with histoplasmosis. There are indications that in North American blastomycosis the internal organs can resist the infection sufficiently to become entirely cleared and apparently subsequently to be immune to reinfection, while the skin does not completely succeed, and remains infected chronically for years. In sporotrichosis the body almost always resists the infection well enough to keep it limited to a single limb, but cannot usually completely eliminate it without medication. Actinomycosis presents all of the phenomena associated with other diseases acquired endogenously, that is from organisms commonly carried by normal individuals without becoming pathogenic.

The systemic mycoses have been discussed first, because they offer more tempting bait to entice immunologists who desire to discover how to save human lives in numbers. However, there are very interesting clues to be found also in the immunologic manifestations of superficial fungous infections of the skin, the dermatophytoses. Consider the significance of the fact that the spouse of a person infected with *Trichophyton rubrum* seldom acquires the disease, even while living for as long as thirty years in a sea of spores contributed to the environment by the partner. The rarity of such transmission led me to estimate that probably only one or two per cent of the population could be infected by this organism, even if it were inoculated purposefully into the skin, and that therefore these few must present some abnormality of the skin. Even more interesting is the fact that persons related by blood to such an infected individual more often become infected if living with him, indicating that his immunologic abnormality may be a defect transmissible genetically. In this disease there is one disconcerting and, to me, utterly astounding fact, in that some 20 per cent of persons infected chronically for many years may have the disorder on one hand or one foot only, without ever infecting the other. This could be a very valuable clue to other discoveries, such as resistance or susceptibility being localized in certain tissues or areas.

In favus, caused by *Trichophyton schoenleini*, a similar genetically transferable tendency seems evident, also in tinea versicolor. These and other examples indicate that fungous diseases become lethal or chronically persistent only in persons who are not normal with respect to immunologic mechanisms of resistance. It is not too much to expect that adequate study of such individuals will eventually yield these secrets.

Although many drugs have been discovered which are capable of killing or inhibiting the growth of pathogenic fungi *in vitro*, none has as yet been capable of curing all cases of the serious deep mycoses, nor the extremely chronic forms of the superficial group. It is becoming ever more evident that if we are to succeed in achieving permanent cure we must try instead to find how we can return the infected individuals to a normal immunologic status. If we can learn to do this, such understanding of these apparently comparatively simple mechanisms should point the way in a manner helpful to the solution of the immunologic control of the infectious scourges of man which have by no means been permanently vanquished, but are only bowing temporarily in submission to present-day drugs.

At the clinicohistopathologic conference of the American Academy of Dermatology last year, Dr. Hamilton Montgomery presented the case of a 9 year old girl who has had severe moniliasis for several years. In asking me for discussion, Dr. Montgomery honored me with the title of Mycologist, which I have never claimed. In responding, I stated that the patient needed more than a mycologist, because the fungi which were found associated with her disease were almost certainly no more virulent than those which I am able to culture frequently from my own gastrointestinal tract, or from that of many other healthy individuals with regularity. It was evident that what she needed was a doctor who could discover wherein she was abnormal, and therefore unable to resist these organisms. Only by correcting this abnormality could she be made healthy with any hope of permanence, since even if a drug should be able to kill all of her fungi, she would almost certainly soon be reinfected, and if her

deficient immunologic status remained unchanged, the disease would recur in full force. Her blood serum was found to be deficient in certain amino acids, notably threonine, glutamic acid, and histidine. It would be too good to be true to find such a simple explanation for an immunologic imperfection, yet it might well be that the gamma globulin of the particular shape and size needed to act as an antibody against a disease might require larger amounts than are available of just such building blocks.

The scientific workers of the world have been spending too large a proportion of their time and energy in studying bugs and drugs, and should now revert in large part to studying the mugs, lugs and pugs, and perhaps even the thugs who present these intractable diseases to find where they deviate from the normal and how we can return them to normal. Until that victory is won, we shall never eliminate contagious disease, but only possibly succeed in controlling it through continued vigilance. In this battle, clinicians must enlist in full force, by observing and studying intensively those cases of infectious diseases presented to them, which in the final analysis represent a series of human experiments provided by Nature of a type and degree which would never be attempted by scientific investigators themselves.

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Effect of Lecithin Feeding on Serum Lipoproteins*

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Science is still a long way from explaining the relationship of the lipoproteins to atherosclerosis. Studies reported here and related ones may eventually become a part of the mosaic which gives the final answer.

Introduction

GOFMAN AND ASSOCIATES,[1,2] employing their ultracentrifugal technic, have observed that a certain class of serum lipoproteins appears to be intimately related to the incidence of atherosclerosis. These are present in the so-called low-density lipoproteins of serum, which can be separated by fractional centrifugation after adjusting the serum to a specific gravity of 1.063 with a more dense sodium chloride solution. Flotation of lipoproteins occurs in this process because the final mixture of serum and salt solution has a density greater than that of the lipoproteins. Thus, rather than sedimentation taking place, the lipoprotein molecules actually are displaced in a direction opposite to the centrifugal field. Once isolated, these "low-density lipoproteins" can be separated into classes or groups by means of an analytical ultracentrifuge in which they are subjected to centrifugal forces of 200,000xg in a sodium chloride solution of specific gravity 1.063. With precision photographic data obtained during centrifugation, it is possible to quantitate the levels of these different classes of lipoproteins in serum. Based on their relative flotation rates, the various classes have been characterized in terms of Svedberg units of flotation (S°_f) and are indicated by the notations S°_f 0-12, S°_f 12-20, S°_f 20-100, and S°_f 100-400, the ranges in each case referring to the lowest and highest relative flotation rates for the lipoproteins comprising that class. The concentration of each class of lipoproteins is expressed in terms of mg. per 100 cc.

Gofman and associates[1] have demonstrated that in both sexes and in all age groups the S°_f 12-20 serum lipoproteins are present with a much higher frequency and at higher concentrations in patients who have survived a myocardial infarction than in corresponding individuals without known vascular disease. Moreover, in both males and females in all age groups, this lipoprotein class occurs with increased frequency and concentration in other diseases characterized by prematurely intense atherosclerosis (diabetes mellitus, the nephrotic syndrome, hypothyroidism, and hypertension). These observations have led Gofman and co-workers to the thesis that this lipoprotein class supplies the lipid for atheroma formation; and the descriptive term for this class, "atherogenic lipoproteins," has come into more or less common usage.

The relationship between serum lipoproteins and atherosclerosis has been further clarified recently by Hanig and collaborators,[3] who demonstrated the presence of the S°_f 12-100 fraction in excised atheromatous plaques. The S°_f 12-100 fraction was always present in substantial amounts in aortas revealing atherosclerosis, whereas the S°_f 0-12 lipoproteins were almost completely absent regardless of the presence or absence of atheromatous plaques. This observation implies that this latter fraction is unassociated with atherogenesis and is a normal component of serum.

In view of the association of the S°_f 12-20 lipoproteins and atherosclerosis, it is of great practical importance to consider means by

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which the serum lipoprotein spectrum may be altered so as to reduce the atherogenic fraction. Nichols and associates[4] have reported that vegetable fat will effect a decrease in the S°_{f} 12-20 lipoprotein concentration. This effect has been attributed to the unsaturated fatty acids present in the vegetable fat.

Lecithin, one of the group of lipids known as phospholipids, plays an important role in lipid metabolism in liver. Normal lecithin turnover in liver appears in some obscure way to be intimately associated with the ability of liver to oxidize fat and with mobilization of fat from liver to peripheral sites.[5] Since serum lipoproteins are believed to be derived from liver, it is conceivable, in view of this relationship of lecithin to lipid metabolism in liver, that feeding lecithin could favorably alter the serum lipoprotein spectrum. Moreover, since lecithin contains a high percentage of unsaturated fatty acids, primarily linoleic and linolenic acids, it is reasonable to expect, in view of the observation of Nichols and co-workers,[4] that lecithin administration would reduce the S°_{f} 12-20 lipoprotein fraction. Pertinent, also, to a consideration of the possible efficacy of lecithin feeding, is the observation of Ahrens and Kunkel[6] which may be interpreted to mean that serum lipoproteins require a certain complement of lecithin in the lipid prosthetic group for maximum stability.

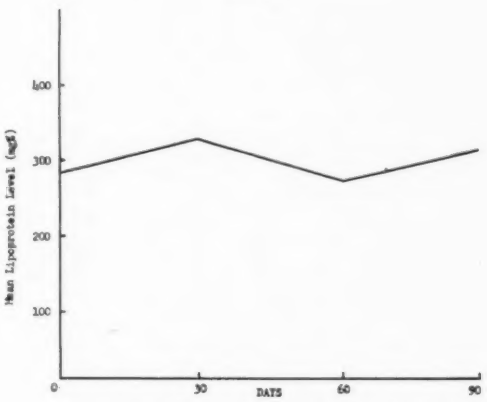
The present study was designed to determine the effect of lecithin feeding on the serum lipoprotein spectrum.

Methods

Nine male patients and 9 female patients ranging in ages from 70 to 90 years at the Norfolk State Hospital in Nebraska were used in this study. All were diagnosed as suffering from psychosis with cerebral arteriosclerosis but were sufficiently cooperative to take oral medication. Blood samples were taken in the fasting state prior to the administration of lecithin,* and then serially every 30 days throughout a feeding period of 90 days. One tablespoon of lecithin three times a day, which amounted to approximately 23 Gm. of lecithin per day, was given as a supplement to the normal ward diet during this period.

*RG Sova Lecithin was kindly supplied by The Glidden Co., Chicago, Ill.

FIG. 1

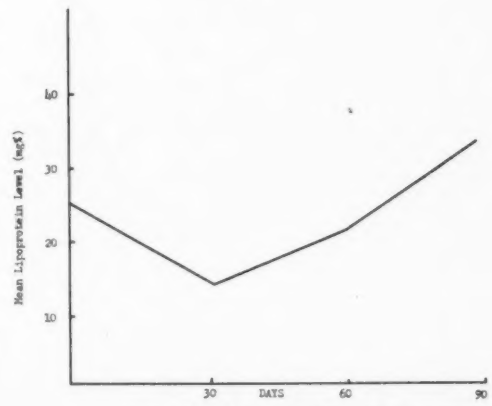


Levels of S°_{f} 0-12 Lipoproteins During Period of Lecithin Feeding in Total Patient Group

Results

The S°_{f} 0-12 serum lipoprotein fraction does not appear to be altered by the feeding of lecithin. Figure 1 shows the average value for this fraction in the entire group of patients at the end of each of the 30 day intervals. Statistical analysis of these data by the method of Grant[7] shows that the changes with time are not significant. Figure 2 presents the corresponding data for the S°_{f} 12-20 fraction. A definite lowering of this fraction during the first 30 days was observed with a return to above the initial level by the end of the 90 day period. This lowering with the subsequent rise has been found to be significant according

FIG. 2



Levels of S°_{f} 12-20 Lipoproteins During Period of Lecithin Feeding in Total Patient Group

to Grant's parabolic F trend analysis[7] and was also characteristic of the male and female groups when analyzed separately.

In neither the S°_f 0-12 nor the S°_f 12-20 lipoprotein fraction was a significant difference in trend between men and women patients observed. However, a sex difference was observed in the case of the S°_f 12-100 fraction. In figure 3 it is apparent that the level of the S°_f 12-100 fraction in men was considerably higher than in women initially, and decreased significantly in men during the 90 day feeding period. The effect of lecithin feeding was quite the opposite in the female group, causing a significant increase in this fraction. Analysis of these data for both female and male groups revealed a statistically significant linear trend.

Four of the men studied appeared to be more alert toward the end of the study. The systolic and diastolic blood pressures were progressively lowered in 14 of the 18 patients during the 90 days of lecithin feeding.

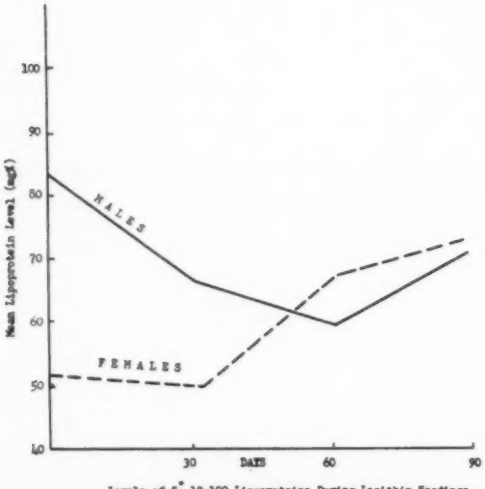
Discussion

The results of this study reveal that a dietary supplement of lecithin produces a sharp decline in the S°_f 12-20 fraction of serum during the first 30 days with an eventual rise to above normal levels by the end of the following 60 days. These data suggest that since lecithin feeding will transiently lower the atherogenic lipoprotein fraction, intermittent administration of lecithin would retard atherogenesis. In this connection it is of interest that Steiner and Domanski[8] have observed a marked lowering of serum cholesterol after 35 days of lecithin feeding. Since Hanig and associates[3] observed the presence of the S°_f 12-100 lipoprotein fraction in atheromatous plaques, the potential therapeutic value of lecithin in the male, at any rate, is further indicated by the reduction in the S°_f 12-100 fraction produced by lecithin feeding. The opposite effect of lecithin on this fraction in women may be related to their substantially lower initial level of S°_f 12-100 lipoproteins.

In contrast to the S°_f 12-20 and S°_f 12-100 lipoprotein fractions, the S°_f 0-12 fraction, which exhibits the lowest flotation rate, showed no change in concentration following lecithin administration. This suggests that no appreciable conversion of other fractions into this fraction occurred and that it is the most stable fraction of the entire lipoprotein spectrum.

It is important to note that the patients in this study range in age from 70 to 90 years. Lipoprotein levels of individuals in this age bracket have been shown by Chapman and collaborators[9] to be as low as levels observed in the 20 to 29 year age group. The levels reported in this study are in agreement with those of Chapman and his group. It is conceivable that if subjects with higher lipoprotein concentrations, such as normal middle-aged subjects or patients with diabetes mellitus, hypothyroidism, or myocardial infarction, had been employed in this study, the changes following lecithin feeding would have been more striking.

FIG. 3



Levels of S°_f 12-100 Lipoproteins During Lecithin Feedings in Male and Female Patient Groups

Summary

A group of aged male and female patients with a diagnosis of psychosis with cerebral arteriosclerosis, who were fed a dietary supplement of lecithin for a period of 90 days, demonstrated a definite lowering of serum S°_f 12-20 lipoprotein concentration followed by a return to above the initial level at the end of the feeding period. The S°_f 12-100 fraction was observed to decrease in concentration in the male patients but increase in female patients. The S°_f 0-12 lipoprotein fraction remained unchanged in concentration during the experimental period.

In view of the ability of lecithin to transiently reduce S°_{f} 12-20 lipoprotein concentration, it is suggested that intermittent lecithin feeding may retard atherogenesis.

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Discussion (Abstract)

Dr. Merritt W. Foster, Jr., Richmond, Va. I would like to compliment Dr. Barak and his fellow authors on presenting an interesting paper from the standpoint of their approach. This particular method of studying the management of the aged psychiatric patient indicates a continued trend in the closer relationship of neuropsychiatry and biochemistry. The field of neuropsychiatry has in recent years become closely allied with many other related fields, particularly in the realm of the social sciences, and it is stimulating to see a continuing alliance with the physical sciences as well.

I had hoped that there would be more discussion and correlation of clinically observed behavior with lipoprotein alteration and would be interested if the authors could elaborate on this point beyond the information given in the paper.

I would also be interested in a discussion of the dietary intake of the patients involved in the study. This could be a very pronounced and possibly deciding factor in the values obtained unless the diet were constant throughout the study.

Finally, it is interesting to note, as demonstrated in figure 3, that the lipoprotein in females of this aged group does not closer approach that of the males. This is particularly interesting since blood cholesterol in the two sexes does approach the same figure in older people. It is generally accepted that blood cholesterol levels in females prior to the menopause is definitely lower than that of males but following the menopause approaches the same level. I would be interested in the authors' comments on this apparent disparity in their findings with lipoprotein changes.

Dr. Cortez F. Enloe, Jr., New York, N. Y. The most significant fact revealed by this research is that this combination of phosphatides—"RG" Lecithin—has, in this instance and under the conditions of this study, demonstrated its ability to alter the lipoprotein pattern of elderly, and presumably, arteriosclerotic patients. In a sense this is not surprising, for our theoretical knowledge of this substance suggests that such results may be expected. If the work is confirmed, we have a new therapeutic or, more accurately stated, nutritional agent for use in the prophylaxis and treatment of this disease.

We would call your attention to the fact that there was an elevation in the mood of these patients. This has been reported previously as a result of lecithin therapy. Unfortunately, there is no biochemical measurement for this phenomenon, but it is significant that a great many investigators using lecithin in elderly patients do notice this subjective response in mood elevation or, better stated, a sense of well-being that ensues.

The substance used in the treatment of these patients was a refined grade of Soya Lecithin. It is the only "RG" type available and is an alcohol soluble RAIG fraction of lecithin, inositol and cephalin phosphatides. It is thus very high in unsaturated fatty acid content which very likely explains its effect we are observing on serum cholesterol.

As we see it, this study demonstrates in a limited manner the fact that "RG" Lecithin can disturb the homeostatic mechanism which is deranged in atherosclerosis. The curious fact here is that these deranged lipoprotein levels tend to shift to more normal patterns, but then return to the more pathologic side on prolonged feeding.

We have asked ourselves why this beneficial effect noted at the thirty day interval does not persist. The only answer we might offer is that the homeostatic mechanism which is deranged in atherosclerosis drifts toward the normal in earlier therapy, then gradually readjusts itself and reverts to the pathologic. It causes us to speculate that in using "RG" Lecithin in the treatment of atherosclerosis, one might feed the phosphatide with interrupted "rest periods." Thus, the inborn defect might not become unresponsive to the therapy.

Intramedullary Fixation of Fractures of the Forearm*

F. WAYNE LEE, M.D., *Charlotte, N. C.*

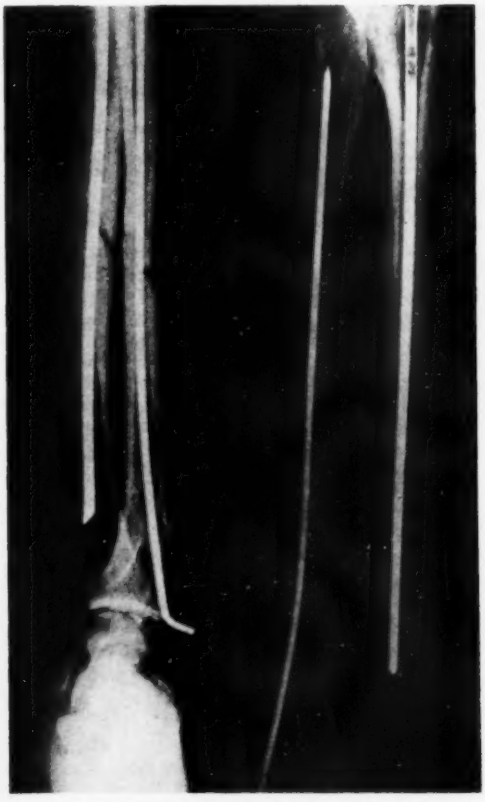
When difficulties are encountered in closed reduction which will interfere with the ultimate ability to pronate and supinate the forearm, open reduction of the fractures is indicated in the opinion of the author.

FRACTURES OF THE SHAFTS of the bones of the forearm in adults continue to perplex surgeons who are called upon to treat them. Although there may be many causes for the failures in reducing and holding these fractures, there is one basic principle which has frequently been overlooked. This is the unique anatomic construction of the forearm as regards pronation and supination, and the attendant rotational deformity which is produced when this relationship is disturbed. This deformity demands the same attention to its correction as does shortening and angulation.

FIG. 1

(Case 1) Fractures of radius and ulna at admission.

FIG. 2



(Case 1) Fixation of fractures using Rush pin in ulna and large wire in radius.

It is a basic assumption in reduction of a fracture that when the proximal fragment cannot be controlled, one brings the distal fragment into line with it. In the fractures

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FIG. 3

(Case 1) Early union 8 weeks later (radius uniting at slower rate).

under consideration here the proximal fragment cannot be controlled. It therefore becomes most important to accurately determine this fragment's position in rotation. This may be accomplished by viewing the shape of the bicipital tuberosity in a true anteroposterior x-ray examination. Those unfamiliar with the use of this technic will find help by comparative views of the normal arm in varying degrees of rotation.

Utilizing these facts, together with all the other sound principles of the technic of reduction, it is reasonable to assume that fractures of the forearm can be successfully handled in a conservative manner, and indeed many of them can be. However, it has been repeatedly observed that a large percentage of poor results may be expected when technics for closed reduction are employed. Knight and Purvis[1] stated in 1949 that by utilizing manipulation as a primary method of treatment they had unsatisfactory results in 71 per cent of cases. They also expressed the opinion that better results would have been obtained had they used open reduction and some form of internal fixation. The course of their patients in whom intramedullary fixation had been used, had not been followed long enough at that time to allow them to properly evaluate this method of treatment.

Present Study

The method of internal fixation employed in this small series of fractures was the use of a Rush pin for the ulna and either a Rush pin or a Kirschner wire of large caliber for the radius. With rare exception manipulation under anesthesia with immobilization by cast was used as a primary method of treatment. From a series of 25 cases which have been treated during a 5 year period, I have selected

FIG. 4

(Case 2) Segmental fracture of radius and simple fracture of ulna. Manipulation had been unsuccessful.

FIG. 5

(Case 2) Six weeks after intramedullary fixation of radius. Early union is apparent.

representative cases which demonstrate some of the peculiar features of this form of fixation. Of the 5 cases presented, 3 had other serious injury which precluded early operation. The other 2 were treated initially by manipulation by other surgeons and the internal fixation under my supervision was necessarily delayed.

The technic employed was a direct approach to the fragments through standard incisions. Retrograde cannulation of the medullary canal was used for the ulna. In addition to direct visualization of the radial fragments, the radial styloid was exposed through a small transverse incision. The wire or pin was inserted through a drill hole placed as near parallel to the shaft as possible. The pins were bent as necessary to gain rigid fixation. Immobilization by plaster was used except in the first case. Firm union was not demonstrated before 14 weeks in any case. There were no wound infections in this series. Postoperative range of motion could not always be adequately measured due to other complicating injury about the wrist or elbow. However, it approached normal in those instances which could be suitably evaluated for the particular functions of flexion, extension, pronation, supination and radial and ulnar deviation.

Case Reports

Case 1. R. L., a 22 year old white man, was admitted to the Charlotte Memorial Hospital on February 3, 1952, after having been injured in an automobile accident. He had a fracture of his right femur, soft tissue lacerations, and the fractures of the bones of the forearm as demonstrated in figure 1.

The patient's condition allowed for immediate orthopedic treatment and accordingly manipulation was

FIG. 6

(Case 2) Complete union at 5 months.

FIG. 7

(Case 3) Position 3 weeks after injury; reduction lost with poor position of fragments.

used as the choice for handling the fractures of the forearm. On the 4th hospital day he developed respiratory complications and other clinical phenomena compatible with fat embolism. His condition remained precarious for the next 10 days, and at the end of that time new x-ray studies demonstrated that the reduction was unsatisfactory.

The patient was considered a candidate for intramedullary fixation and the operation was done without incident. Figure 2 demonstrates the immediate postoperative result. This was the first patient I had treated with pins and I did not use immobilization by plaster. I was anxious to know if external support would be advantageous in a patient who would be relatively inactive, and I wished to see if rigid internal fixation would not in itself be sufficient to guarantee union. Eight weeks following operation it was noted that union was occurring at a normal rate although it should be recognized that the radius was uniting more slowly than the ulna (Fig. 3). The pins were removed about 7 weeks later and the patient was last examined on September 18, 1952. At that time the motion of the forearm was near normal in all ranges.

Case 2. J. E., a 40 year old white woman, was injured while working in a textile mill. She had a fracture of the ulna near the junction of the middle and distal thirds, and a segmental fracture of the radius (Fig. 4). The patient was first treated by her family surgeon who, using manipulation, was unable to procure alignment primarily because of the comminution of the radius.

The patient was referred for further treatment; it was decided that the fracture could be managed best by intramedullary fixation. A large caliber Kirschner wire was used when a Rush pin proved too large for insertion. It was not felt necessary to fix the ulna because of the good position obtained after the radius had been aligned. Figure 5 demonstrates the position with beginning callus at 6 weeks; figure 6 shows the solid union which was apparent in 5 months. This patient was evaluated several years after the injury and was found to have an excellent range of motion in both wrist and elbow.

Case 3. F. R. M. was seen initially on February 23, 1953, after his left forearm had been caught in a piece of heavy machinery. It was related that his

FIG. 8

(Case 3) Four months after fixation, radius solidly united and ulna partially united.

FIG. 9

(Case 4) Position in right forearm is satisfactory after closed reduction.

arm had been pulled into the rotating bars of the machine and, in addition to the fracture of the forearm, that he had a compound fracture-dislocation of the elbow. The initial treatment included debridement, reduction of the elbow, and manipulation of the forearm. X-ray films obtained immediately after operation demonstrated a satisfactory reduction of the radius and ulna. Three weeks later a new set of films revealed that the fragments had slipped and that the position was now completely unsatisfactory (Fig. 7). (This demonstrates a feature that is often overlooked in reductions of the bones of the forearm, namely the desirability of checking the position of the fragments by x-ray examination after ten days or two weeks of immobilization.)

The elbow wound had healed sufficiently by this time to allow open reduction of the fractures of the forearm. The fragments were exposed in the proximal forearm only, the distal ulnar fragment being pinned blindly. Four months following the accident x-ray films demonstrated solid union in the radius and partial union in the ulnar (Fig. 8). The pins were removed after another 6 weeks. The end result as regards pronation and supination is only fair; the hand is also partly disabled by damage to the nerve at the elbow.

Case 4. S. S. was admitted to the hospital on May 8, 1953, after the car in which he and three other college students were riding careened over a steep embankment. His injuries consisted of a compound fracture of the left femur, bilateral fractures of the bones of both forearms, a dislocation of the left shoulder, a compound fracture of the distal right humerus, multiple pelvic fractures, a severe laceration and avulsion of the palmar surface of the right hand, and severe shock.

Immediate treatment for the forearms consisted of simple immobilization. When the patient's condition had stabilized to permit a short anesthetic, the right forearm was manipulated for reduction. A short cast was used to utilize a wire through the olecranon for traction on the comminuted distal end of the humerus. The fragments in the forearm were felt to be in good position (Fig. 9). Three months after this treatment the x-ray studies demonstrated early union at the fracture sites (Fig. 10).

The left forearm was manipulated and immobilized at the same time as the right but the position was not maintained. Intramedullary fixation was used and after 4 months it was felt that union was complete in the radius and at least partially so in the ulna (Fig. 11). Shortly after this the pins were removed to accommodate the patient who was moving to another city. In a few weeks he returned demonstrating a frank nonunion in the ulna (Fig. 12). A new cast

FIG. 10

(Case 4) Position maintained and union progressing normally after 3 months of plaster immobilization.

FIG. 11

(Case 4) Left forearm 4 months after internal fixation; union complete in radius but incomplete in ulna.

was used for three months but the nonunion persisted and intramedullary fixation was employed. In this instance a Rush pin was used and cancellous bone was taken from the ilium to serve as graft material. Six months following operation x-ray films demonstrated solid union of the ulnar fragments.

Case 5. J. C. was treated in a neighboring city for a fracture of the radius and ulna sustained in an accident in a textile plant. In the anteroposterior view it can be seen (Fig. 13) that the upper portion of the forearm is in complete supination while the distal forearm is in midposition. (This demonstrates the principle which must be remembered in realigning the distal fragment to the supinated proximal radius.) Following reduction by his family surgeon partial correction of the distal pronation was secured. Immobilization was maintained for 6 months using a long arm cast. At the end of this time it was found that the radius had united with some malalignment, but the ulna showed a nonunion (Fig. 14).

The patient was treated by intramedullary fixation of the ulna utilizing cancellous bone for the graft (Fig. 15). Union was complete after 5 months. The pins were removed after ample time had been allowed for rehabilitating the wrist and elbow. The end result was satisfactory, although at the last examination both pronation and supination were limited in the final 20 degrees.

Discussion

The ordinary complications attendant to open bone surgery will apply to these fractures of the forearm. The operation should not be attempted by those unfamiliar with open reduction technics. Pins must be chosen for proper length and diameter and the principle of dynamic splinting by three point

FIG. 12

(Case 4) Ulna shows nonunion after removal of pins; further surgery required by premature removal of internal fixation.

FIG. 13

(Case 5) The rotational deformity with proximal fragments in partial pronation is shown.

fixation as advocated by Rush must be kept in mind. Wandering of the pins will not occur and breaking and bending will not be seen if basic principles are observed.

It is now recognized that fractures treated by this method will almost invariably demonstrate slow union. This is no doubt related to the periosteal stripping and the endosteal disturbance that occurs at the time of operation. It appears that 16 weeks is the minimum time for solid union. In addition to rigid fixation of the fragments and proper immobilization by cast, one should consider using cancellous bone to reinforce the fracture site. The iliac crest offers the ideal site for donor bone.

In a small percentage of the cases treated it was noted that the patients developed a transient tenosynovitis of the long abductor and extensors of the thumb. This was felt to be the result of irritation to the tendon sheaths produced at the level of the radial styloid during the insertion of the radial pin. It is recommended that careful placement of the pin be guaranteed by adequate exposure and that the curved end of the pin be kept free of contact with the tendon sheaths. No permanent damage of tendon or tendon sheath has been encountered.

FIG. 14

(Case 5) There is nonunion of ulna after 6 months in a plaster cast; the radial union is firm but with malalignment.

FIG. 15

(Case 5) Union of ulna shown 5 months after internal fixation and bone graft.

Summary

Fractures of the shafts of the forearm bones can be satisfactorily treated by closed manipulation providing both axial and rotational alignment is procured and maintained in every case. Extraneous factors may make it necessary to utilize open reduction and internal fixation. In such cases intramedullary pins will fulfill the requirements for proper management of these problems. Since union will often be delayed following the use of this type of fixation, the use of accessory bone is recommended to bring about earlier consolidation. External fixation with plaster would seem to be necessary and should be continued until solid union is demonstrated by x-ray examination. Removing the pins prematurely is hazardous and should be condemned. Fixation of the fragments must be rigid and can be assured by choosing proper pins which may be bent to gain physiologic and anatomic advantage. In certain instances it is adequate to utilize internal intramedullary fixation in only one of the involved bones utilizing such fixation to gain length and thus aid in aligning the unpinned bone. Further investigation will be needed combined with a larger series of cases to properly evaluate this form of treatment. At the present time it would seem to be deserving of continued use.

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A Comparative Study of Hexylcaine, Procaine, and Lidocaine with Specific Attention to Tissue Irritation*

CLAUDE A. TAIT, M.D., NORMAN O. REESE, M.D., and DAVID A. DAVIS, M.D.,† *Chapel Hill, N. C.*

The authors question the use of Hexylcaine in conduction anesthesia. Their studies demonstrate the irritative properties of this drug.

IN ITS COURSE from synthesis to clinical usage, Hexylcaine has stood and passed the conventional rigid trials demanded for the acceptance of a new drug. It has established itself as a local anesthetic of low relative toxicity, considerable stability, prolonged duration, superior potency and versatility.

Curiously wanting have been cogent evaluations of its effect upon the tissues injected. To be sure there is negative evidence extant in the literature, by virtue of a failure to mention inflammatory complications, bearing on this point.

The fundamental research concerning Hexylcaine was done by Cope and Hancock, 1944[1] and Beyer and Latven, 1948, 1950.[2,3] Various clinical and comparative studies by Wylde, Waters, and Orth,[4] Ruben and Anderson,[5] Torkelson and Cooley,[6] Orkin and Rovenstine,[7] Crawford,[8] Reich,[9] Arcuri and Newman,[10] Jacques and Hudon,[11] Lubowe,[12] Ansbro and associates,[13] and Blundell and collaborators,[14] established this agent as one capable of safe and effectual administration by any conventional route. In most studies Hexylcaine compared favorably with other popular agents of current usage.

Although none of the above authors reported tissue irritation incident to the use of Hexylcaine, our earliest efforts to exploit its versatility were met with complaints of immediate and prolonged burning at the site of injection. There followed a succession of patients who manifested heat, swelling, pain and tenderness, the classical picture of inflammation, in areas infiltrated with 1 per cent Hexylcaine, and complaints of smarting upon topical conjunctival application were not wanting.

These experiences provoked our study of the irritating potentialities of this otherwise effective drug, and to determine whether or not this drug was in fact an "anaestheticum dolorosum," for the above described effects were those which prompted Hertzler (quoted by Meeker, 1928[15]) to coin the term.

The following studies were made: (1) intradermal injections in man with gross observations; (2) intradermal injections in rabbits with gross and microscopic observations; (3) direct and blind sciatic nerve injections in rabbits with microscopic examinations of tissue; (4) conjunctival tests in rabbits with gross evaluation; and (5) injections into the anterior chamber using rabbits, again with gross evaluation.

The solutions employed in this comparative study were (1) procaine hydrochloride, 1 per cent, (2) Hexylcaine hydrochloride, 1 per cent, (3) Lidocaine hydrochloride, 1 per cent, and (4) sodium chloride, 0.89 per cent. These were numbered and unknown to the examiners and subjects.

The compositions and properties of the preparations used are shown in table 1.

Method

1. *Intradermal Wheals in Humans.* Ten healthy adult house officers and medical stu-

*Read before the Section on Anesthesiology, Southern Medical Association, Fiftieth Annual Meeting, Washington, D. C., November 12-15, 1956.

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TABLE 1

COMPOSITION AND PROPERTIES OF SOLUTIONS

Solution	*Concentration*	*pH*	*Mol. Wt.*	*Preservative*	*Tonicity*	*Solvent*
Procaine HCl	1%	2.87	236.3		Isotonic	NaCl
Hexylcaine HCl	1%	3.66	297.81	0.15% Methyl Paraben	Isotonic	H_2O
Lidocaine HCl	1%	6.49	234.33	0.1 % Methyl Paraben	Isotonic	NaCl
NaCl	0.89%	7.0	58.45		Isotonic	H_2O

dents were subjected to the intradermal injection of 0.5 ml. of each of the test solutions on the volar surface of the forearm by means of 26 gauge needles. Gross observations were made as to swelling, redness, heat, and tenderness at ½ hour, 24, 48, and 72 hours, and later when justified. The degree of inflammation was judged as follows:

0 None.
1+ Edema zone of 2 to 5 mm. in diameter.
2+ Edema zone exceeding 5 mm. with mild redness.
3+ Redness exceeding 5 mm. with heat and tenderness.
4+ Evident necrosis.

To exclude the possible effects of age and deterioration, comparative dermal wheals were made in an additional group of 5 volunteers, using samples from the stock and manufacturer's lots of Hexylcaine alone.

2a. *Intradermal Wheals Using White Rabbits.* This test as described by Hoppe and associates[16] was modified by the intravenous administration of T-1824 (Evans Blue). The abdominal skin of 9 white rabbits was carefully shaved and cleansed; 0.2 ml. of each test solution was injected intradermally through 26 gauge needles. Thirty minutes thereafter, T-1824 was given intravenously in quantities of 1 ml./Kg. of an 0.5 per cent solution. Observations regarding the physical signs of inflammation and the quantitative uptake of T-1824 were made at 15 minutes, 30 minutes, 1, 2, 3, 24, and 48 hours. The gross inflammatory changes were rated as were those in humans, and the dye uptake in the following manner:

0 No dye present.
1+ Faint bluish hue.
2+ Evident blueness 1 to 5 mm. in diameter.
3+ Marked blueness 1 to 5 mm. in diameter.
4+ Extensive blueness or marked blueness exceeding 5 mm. in diameter.

2b. *Microscopic Examination of Dermal Wheals in Rabbits.* Four of the rabbits used in Experiment 2 were chosen at random and sacrificed after 48 hours, using intravenous thiopental. The dermal wheals were widely excised and separately fixed in 5 per cent formaldehyde, processed in the usual manner, and stained with hematoxylin and eosin. Several sections cut through each wheal were examined microscopically with specific regard to edema, cellular response, and necrosis. Grading of the inflammatory responses on a quantitative basis would necessitate a detailed discussion of variables such as intensity of the stimulus, time intervals and the very controversial sequence of inflammatory events and their relation to one another. Present knowledge does not permit the process of inflammation to be quantitated and any assessment beyond such crude statements as "more" or "less" inflammation would constitute fictitious accuracy. The degree of inflammation was considered zero when the tissue revealed no changes and 4+ when evident necrosis prevailed. From 1+ to 3+ the gradation was one of increasing edema and cellular aggregation. No attempt was made to estimate the degree of acute inflammation which might have preceded a certain degree of fibroplasia.

3a. *Sciatic Nerve Injections Under Direct Vision Using Rabbits.* The sciatic nerves of 5 white rabbits were exposed with minimal surgical trauma, the animals having been anesthetized with sodium pentobarbital. An injection of 0.2 ml. of each test solution was made into a selected nerve trunk and a remaining 0.3 ml. infiltrated into the adjacent areolar tissue. The level of injection was marked by a fine silk suture placed superficially in the muscle thus isolating it from the site of injection. The animals were sacrificed on the tenth day using intravenous thiopental and en-bloc specimens of the sites of injection (to include nerve, connective tissue, muscle, and skin) were fixed and processed in the conventional manner. The sections were stained with hematoxylin and eosin as well as with Mallory's aniline blue. The degree of inflammation of non-nervous tissue was judged in the manner outlined in Experiment 2b. Specific neural damage was assessed according to the presence and

degree of axonal swelling and disruption, myelin fragmentation and proliferation of Schwann Cells.

3b. *"Blind" Sciatic Nerve Injections in Rabbits.* The procedure differed from that outlined under Experiment 3a insofar as: (1) The test solutions were injected percutaneously following landmarks established during the course of direct injection. The adequacy of the blocks were evaluated by practical clinical criteria. (2) The quantity of each solution injected was 1.0 ml. (3) The animals were sacrificed on the seventh day.

4. *Conjunctival Application in Rabbits.* In 4 unanesthetized white rabbits, 0.25 ml. of a test solution was dropped into the conjunctival sac, and the lids held shut for one minute. Observations as to lacrimation, conjunctival injection, and chemosis were made at 15, 30, 45, 60, and 90 minutes. To establish a definite endpoint, 0.25 ml. of 2.5 per cent thiopental, an established conjunctival irritant, was instilled in the same manner in a separate group of rabbits. The immediate violent tearing, injection and chemosis was then regarded as 4+.

5. *Anterior Chamber Injections in Rabbits.* The technic described by Spencer, Sheie, and Dripps,[17] was applied to 12 white rabbits. After anesthetization with 2.5 per cent thiopental and the topical application of 0.2 ml. of 1 per cent tetracaine hydrochloride (shown by pilot studies to be nonirritating in this concentration), 0.1 ml. of a test solution was introduced into the anterior chamber of the eye by means of a 26 gauge needle.

The degree of corneal opacification was recorded at 4 and 24 hours according to the criteria established by the originators of this test, viz.:

0 Cornea clear and transparent.
1+ Faint corneal haze, iridial detail apparent.
2+ Moderate corneal haze, slight iridial blurring.
3+ Dense corneal haze, no iridial detail apparent.
4+ Dense white corneal opacification.

Results

1. *Intradermal Wheal in Humans* (Table 2).

a. At 30 minutes, 13 subjects injected with Hexylcaine displayed areas of redness and swelling at least 5 mm. in diameter, and the remaining 2 volunteers had less severe reactions. Of 10 subjects, one manifested no response, 7 a very minimal one, and 2 could be classed as 2+ in response to procaine. Lidocaine produced no inflammation in 6 instances, 1+ in 3 cases, and only once a 2+. No reactions were observed in control saline wheals.

TABLE 2

DERMAL WHEALS IN HUMANS

Subject	Procaine 1% 30 min.	Procaine 1% 24 hrs.	NaCl 0.89% 30 min.	NaCl 0.89% 24 hrs.	Lidocaine 1% 30 min.	Lidocaine 1% 24 hrs.	Hexylcaine 1% 30 min.	Hexylcaine 1% 24 hrs.
1	2+	0	0	0	1+	0	3+	2+
2	1+	0	0	0	0	0	3+	2+
3	1+	0	0	0	0	0	3+	3+
4	1+	0	0	0	0	0	3+	2+
5	1+	0	0	0	0	0	3+	1+
6							3+	2+
7							3+	2+
8							3+	2+
9							3+	2+
10							2+	1+
11	2+	0	0	0	1+	1+	3+	2+
12	1+	1+	0	0	2+	0	3+	3+
13	0	0	0	0	1+	0	3+	2+
14	1+	0	0	0	0	0	2+	1+
15	1+	0	0	0	0	0	3+	3+

b. Reaction at 24 hours. Only 3 of the 13 severer reactions to Hexylcaine remained 3+ while the remainder showed a clear tendency to abate. It is notable that none of Hexylcaine-induced inflammatory changes were entirely reversed by 24 hours while only one wheal persisted in minimal traces for procaine and Lidocaine.

c. Persistence of reaction. Continued observations showed the lone remaining reactions to Lidocaine and procaine to fade entirely by 48 hours while 3 subjects showed a marked chronicity of the Hexylcaine-induced reaction. Although 12 injection sites had cleared at the end of 7 days during which the erythema and edema were succeeded by induration and hypesthesia, the remaining 3 sites persisted. In these there developed a tawny discoloration with residual induration and numbness. In 2 subjects this effect remained for several months (Fig. 1).

A comparison between two lots of Hexylcaine used in the series did not disclose differing responses.

2a. *Intracutaneous Injections in Rabbits Followed by T-1824 Intravenously.* None of the test solutions failed to elicit some swelling and dye accumulation at the site of the wheal. When saline or Lidocaine were injected, these phenomena were delayed in their

FIG. 1

Dermal wheals 5 weeks after injection of 1% Hexylcaine HCl.

appearance, modest in extent, and fleeting in duration. The responses to procaine tended to appear earlier but were mild and persisted only for 24 hours. The injections of Hexylcaine invariably provoked an evident swelling and accumulation of dye in 30 minutes with continued progression over 3 to 4 hours and a persistence to 48 hours. Hence, as in man, it appeared that Hexylcaine was the most irritating of these agents and procaine and Lidocaine, in that order, considerably less noxious.

2b. *Histological Study of Dermal Wheals in Rabbits.* When present, the degree of dermal inflammation varied from minimal vascular congestion and edema to a moderate leukocytic infiltration. No overt necrosis was observed, nor had sufficient time elapsed for reparative activities.

A minimal amount of edema was observed in all sections irrespective of the injectant. This finding was attributed to trauma by the needle. Procaine appeared to provoke a very modest cellular response while none was observed with Lidocaine. Hexylcaine consistently evoked cellular infiltration of moderate

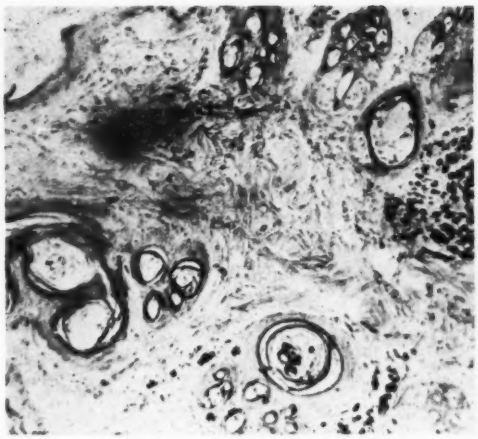
TABLE 3

HISTOLOGICAL STUDIES IN RABBIT SKIN WHEALS

	Procaine 1%		*NaCl 0.89%*		*Lidocaine 1%*		*Hexylcaine 1%*	
Rabbit	*E**	*C†*	*E*	*C*	*E*	*C*	*E*	*C*
A	1+	0	1+	0	0 to 1+	0	2+	1+
B	1+	0	0 to 1+	0	0 to 1+	0	1+	0
C	1+	1+	0 to 1+	0	1+	1+	2+	2+
D	0 to 1+	1+	0 to 1+	0	0 to 1+	0	2+	1+

*Edema †Cellularity

FIG. 2

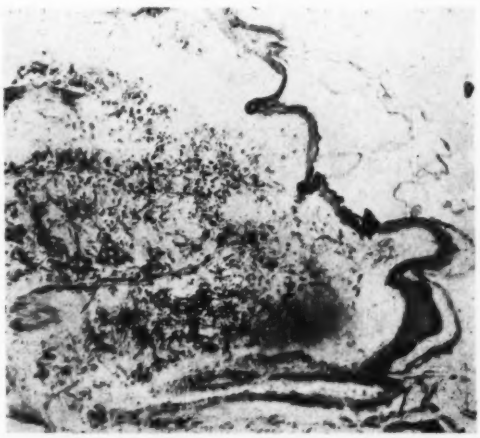


Rabbit dermis injected with isotonic saline.

degree, thus plainly distinguishing itself from the other test solutions (Table 3). The contrasting effects of isotonic saline and Hexylcaine are illustrated in figures 2 and 3.

3. *Sciatic Nerve Injection in Rabbits.* In order to evaluate the specimens derived from the direct and indirect application of the test solutions to the sciatic nerves as one group, only those of the "blind group," which showed obvious sciatic nerve paralysis, were included. To facilitate clarification of the results, the inflammatory changes were separately recorded for, (1) skin, (2) connective tissue (subcutaneous tissue, fat, perineurium,

FIG. 3



Rabbit dermis injected with 1% Hexylcaine HCl.

TABLE 4

HISTOLOGICAL STUDIES OF RABBIT SCIATIC NERVES

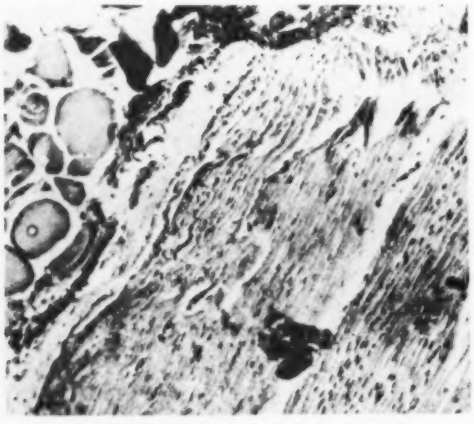
Solution	*Preparation*	*Dermis*	*Conn. Tissue*	*Muscle*	*Nerve*
Procaine 1%	a		1+	0	0
	b		1+	0	0
	c	0	0	0	0
	d	0	0	0	0
NaCl 0.89%	a		0	0	0
	b		0	0	0
	c	2+	0	0	0
	d	0	0	0	0
Hexylcaine 1%	a		1+	0	0
	b		0	0	0
	c	3+	3+	4+	0
	d	2+	2+	2+	1+
Lidocaine 1%	a		0	0	0
	b		0	0	0
	c	0	0	0	0
	d	1+	0	1+	0

a and b—Direct injection.
c and d—Percutaneous injection.

and perimysium), (3) muscle, and (4) nerve (Table 4).

Sodium chloride failed to produce a reaction in any tissue except in one specimen in which a minimal dermal fibroplasia was observed. In response to Lidocaine one specimen revealed the above changes as well as a slight degree of edema in skeletal muscle. The reaction to procaine (Fig. 4), although more severe, consisted only of moderate vascular engorgement and perineurial fibroplasia. In sections from specimens of Hexylcaine-treated tissues, considerable dermal fibroplasia, monocytosis and edema overlay a no less obvious areolar connective tissue reaction and muscle degeneration. The latter consisted of a loss of muscle striations, fibrillar edema, and disruption of architecture (Figs. 5, 6 and 7).

FIG. 4



The perineurial reaction to 1% procaine HCl.

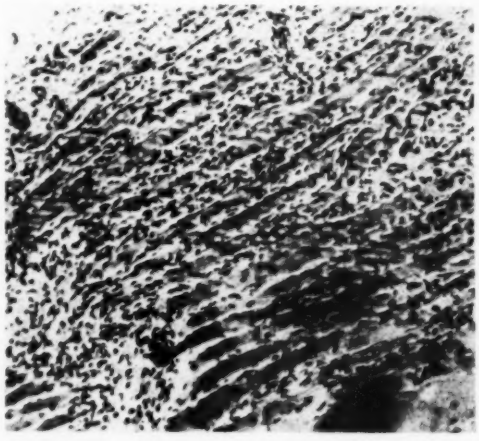
FIG. 5

The response of connective tissue and skeletal muscle to 1% Hexylcaine HCl.

Of interest is the fact that only one section revealed specific axonal involvement. In this instance it consisted of a vague swelling of the axis cylinder. By virtue of its isolated appearance and controversial vagueness, it is considered to be an artefact, and Hexylcaine was thought to produce no axonal changes (Figs. 8 and 9).

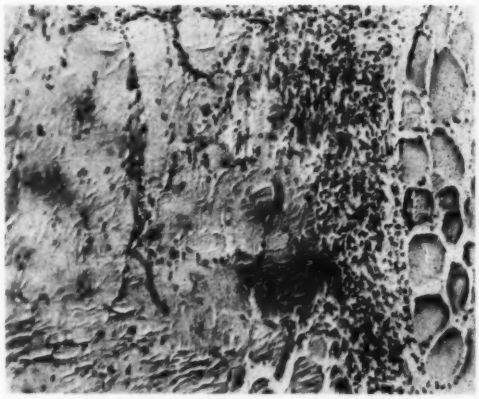
4. *Conjunctival Instillation in Rabbits.* In the concentrations used, none of the anesthetic agents or the control evoked even the

FIG. 6



The response of connective tissue and skeletal muscle to 1% Hexylcaine HCl.

FIG. 7



The response of connective tissue and skeletal muscle to 1% Hexylcaine HCl.

slightest response on topical application to the conjunctiva.

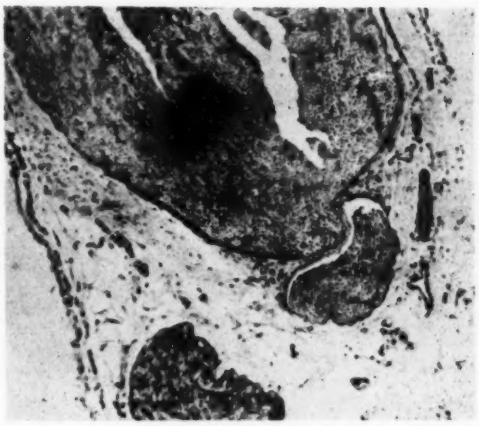
5. *Anterior Chamber Injections in Rabbits.* The deposition of saline, Lidocaine and procaine into the anterior chamber of rabbits' eyes did not provoke any visible corneal changes (Table 5).

In 5 of the 6 globes injected with Hexylcaine, a corneal haze was evident in 3 hours and seen to progress to a density which blurred the iridial detail in 24 hours. The contrast between the saline control and Hexylcaine eyes is shown in figures 10 and 11. The remaining specimen failed to display haziness until some 10 hours after injection and remained faintly hazy for approximately

FIG. 8

Sciatic nerve of a rabbit injected with isotonic sodium chloride.

FIG. 9



Sciatic nerve of a rabbit injected with 1% Hexylcaine HCl.

one week. The more aggravated responses persisted with little or no clearing for at least 3 weeks.

Discussion

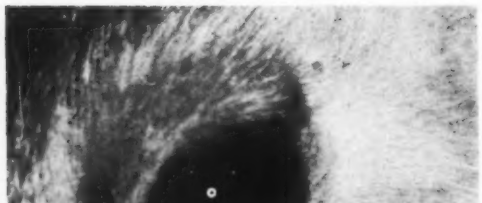
The basic work on Hexylcaine, cited earlier in this paper, did not allude to any tissue irritation incident to its use. Subsequent work by Anderson and Ruben,[18] Blocksma and associates,[19] and Gordon,[20] reiterates complaints by patients of initial and transient burning at the site of injection and residual tenderness for several days following Hexylcaine infiltration. Piro and collaborators[21] describe the occurrence of a slight degree of inflammation following the injection of Hexylcaine into the oral mucosa as determined by biopsy. Our initial experience with burning following infiltration and smarting upon topical application to the conjunctiva and nasal mucous membranes prompted us

TABLE 5

ANTERIOR CHAMBER INJECTION IN RABBITS

	a	*b*	*c*	*d*	*e*	*f*
Procaine 1%						
4 hrs.	0	0	0	0	0	0
24 hrs.	0	0	0	1+	0	0
NaCl 0.89%						
4 hrs.	0	0	0	0	0	0
24 hrs.	0	0	0	0	0	0
Hexylcaine 1%						
4 hrs.	0	2+	2+	1+	2+	1+
24 hrs.	1+	2+	2+	2+	2+	2+
Lidocaine 1%						
4 hrs.	0	0	0	0	0	0
24 hrs.	0	0	0	0	0	0

FIG. 10



Anterior chamber injection of isotonic sodium chloride.

to limit its use. Since that time several personal communications, Moore,[22] Owen,[23] Crawford,[24] and Ruben,[25] have alluded to the possible agency of Hexylcaine in the production of isolated neuritides complicating regional anesthesia.

Our observations on human and animal dermal wheals corroborate the above clinical impressions and microscopical examination of the animal preparations proved these changes to be inflammatory in nature. To be sure, these reactions were not necrotizing or indeed severe, but nevertheless subjectively and objectively more noxious than those produced by other agents of equal therapeutic reputation.

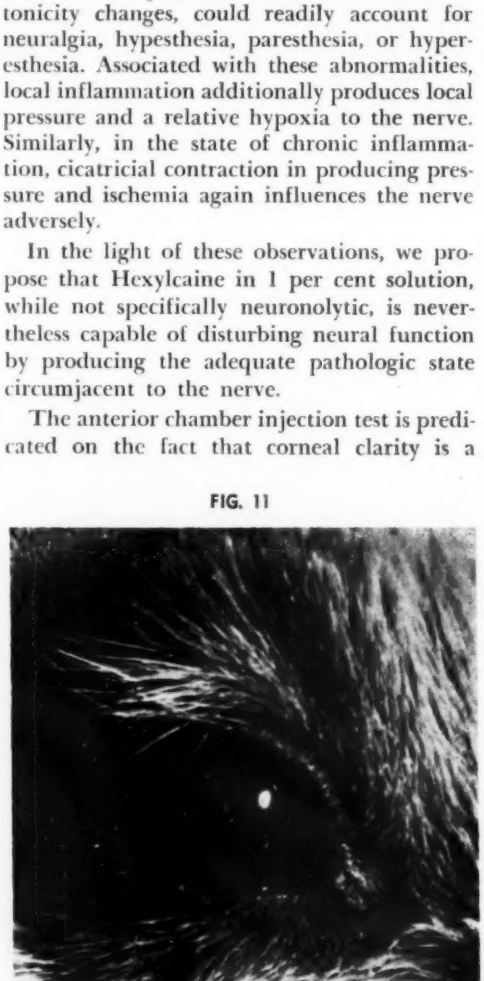
In all our technically satisfactory sections of the sites of injection of the sciatic nerve with Hexylcaine, there was some evidence of inflammation more or less severe. The isolated instance of slight axonal swelling, which can be dismissed as an artefact, indicates that no specific nerve damage was produced with Hexylcaine. However, the degree of perineurial inflammation, in the form of round cell infiltration of the perineurium, nerve bed and adjacent muscle, attended by vascular engorgement and edema occasioned by Hexylcaine, is capable of disturbing function. This effect of Hexylcaine differs from the direct neurotoxicity attributed to "Efocaine" by Nowill, Hall, and Stephen,[26] Mannheimer, Pizzolato, and Adriani,[27] and more recently by Clarke, Morrison, and Roberts,[28] and Deaton, Pautler, and Lund.[29] These authors have given excellent clinical and pathologic data showing that Efocaine was capable of severe destruction of nerve fibers to account for neurologic disturbances or deficits.

No such drastic injury to nerves results from the injection of Hexylcaine. However, the work of Moore,[30] and Womack,[31] presents evidence that the function of a nerve is profoundly altered or disturbed by processes operative in its proximity. They have shown that perineurial inflammation in its exudative stage, bringing about a lowering of pH, an increase in potassium concentration, and tonicity changes, could readily account for neuralgia, hypesthesia, paresthesia, or hyperesthesia. Associated with these abnormalities, local inflammation additionally produces local pressure and a relative hypoxia to the nerve. Similarly, in the state of chronic inflammation, cicatricial contraction in producing pressure and ischemia again influences the nerve adversely.

In the light of these observations, we propose that Hexylcaine in 1 per cent solution, while not specifically neuronolytic, is nevertheless capable of disturbing neural function by producing the adequate pathologic state circumjacent to the nerve.

The anterior chamber injection test is predicated on the fact that corneal clarity is a

FIG. 11



Anterior chamber injection of 1% Hexylcaine HCl.

function of its state of relative dehydration, which in turn is maintained by its epithelium and endothelium. Should the integrity of either barrier be disrupted by physical, chemical, or thermal traumatism, the result would be an imbibition of fluid by the cornea, through either a distinct break in membrane continuity or by transudation permitted by increased permeability. The end result of trauma to the cornea is therefore opacification of varying degrees. Our results, in complete accord with those of the original authors who also employed Hexylcaine 1 per cent, confirm their impression that Hexylcaine possesses a moderately irritating effect upon the corneal membrane.

It is not likely that the apparent effects of Hexylcaine on the cornea are attributable to tonicity, pH, or the preservative. Inspection of table 1 indicates that Hexylcaine, the only agent producing corneal injury, shows isotonicity common to the other test solutions, is within the pH range of procaine (2.8 to 5.5) and contains the same preservative as Lidocaine. Finally, Spencer and associates *(vide supra)*, established the preservative methylparaben as innocuous to tissue.

From the evidence derived from the intracutaneous, neural, perineurial, and anterior chamber injection of Hexylcaine, it is apparent that this drug is not innocuous and the advisability of its use as an agent for conduction analgesia by injection is questionable.

Summary

A comparative study of the possible irritant qualities of Hexylcaine hydrochloride, procaine hydrochloride, and Lidocaine hydrochloride in 1 per cent solutions was made, using isotonic sodium chloride as the control.

By the production of dermal wheals in man and rabbits, with pathologic study applied to the latter, Hexylcaine was shown to be the most irritant of the agents employed.

By direct and indirect sciatic nerve injection in rabbits, Hexylcaine's neurotoxic properties were established as indirect, viz., by the stimulation of perineural inflammation. The effects of perineural inflammation on the function of the peripheral nerve proper are discussed.

Injections into the anterior chamber in rabbits established Hexylcaine to be moderately irritating while the other solutions evoked no response. Such ancillary factors as tonicity, pH, and the action of the preservative were satisfactorily excluded as being of possible consequence.

On the basis of these findings, it is suggested that Hexylcaine hydrochloride be used with great caution, or not at all, in the practice of regional and infiltration analgesia.

Acknowledgments

We express our gratitude to Dr. Clyde Strickland of the Merck, Sharp and Dohme Company for his generosity in supplying the Hexylcaine used in these experiments.

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Residual Spinal Injuries From Automotive Crashes: Biomechanical Considerations of Pre-impact, Impact, and Post-impact Factors Involved in Their Production*

JACOB KULOWSKI, M.D., *St. Joseph, Mo.*

The author considers the mechanical effects of automotive crashes upon the spine. There are certain factors physicians and the public must recognize as predisposing drivers to accidents.

THE INCREASING NUMBER and complexity of injuries due to automotive accidents are causing fraternal, medical, engineering, and medicolegal problems. The residual injuries of the neck and low back offer provocative fields of study in this respect. I hope to relate these injuries to pre-impact, impact, and post-impact factors which governed their production and to clinical life histories. Relevant data were obtained from 250 medical records of patients who comprised about 65 per cent of all those having residual disabilities of the motor or skeletal systems after accidents, as seen by me over the past 9 years up to May 1, 1957. This series includes 100 patients with neck, 100 with low back, and 50 with both neck and low back complaints, respectively, and observed consecutively. Few were seen on the day of accident or shortly thereafter. The duration of symptoms for the majority was a matter of weeks or months. In some it was a year or longer, and up to 17 years in one woman with disability of the neck.

Pre-impact Situation

General statistics. This series represents a fair cross section of the motoring population which becomes involved in injury producing accidents. The sexes were about evenly divided as related to the levels of spinal disability. This differed relative to seating. Men drivers comprised 77.60 per cent; women 22.40 per cent; 50 per cent of the total series were drivers. In the right front seat 12 per cent were men, and 55.55 per cent women. Approximately one-third of the patients occupied this seat. The back seat was occupied by 16.40 per cent of all the patients, the sexes being about equally represented.

Approximately 80 per cent of the vehicles involved were automobiles.

The age ranges of the patients were 15 to 20 years, 11.20 per cent; 20 to 45 years, 61.6 per cent; 45 to 65 years, 23.40 per cent; and 65 to 85 years, 3.8 per cent. Drivers between 20 and 45 years exceeded those between 45 and 60 years in a ratio of 4:1.

Up to now seating has been related chiefly to the potentials of injury of current cabin design which seem to determine the clinical results. However, from the biomechanical standpoint seating posture has other implications of equal or possibly greater significance. Engineers conceive this to represent a basic "mass-spring-system," the elastic quality of the spring action acts to determine the maximum deceleration of the seat passenger in instances where the latter is strapped to the seat, the rider-seat combination remaining intact and connected to the vehicle.

On the other hand, from the biomechanical standpoint, the unrestrained passenger achieves only a labile equilibrium. This requires considerable flexibility of the lumbar spine and related body linkages, as well as coordination and strength of the spinal and adjacent musculature, not to mention the complex needs for getting in and out of vehicles. The full implications of these biomechanical requirements are emphasized in the extraordinary instability of the body mass and masses under crash conditions. Moreover, seating imposes certain static detrimental

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Fiftieth Annual Meeting, Washington, D. C., November 12-15, 1956.

loads: namely, stresses of retropulsion on the posterior interspinal ligaments via movements of the intervertebral disc (Keegan[1]); increased tensile stresses upon interlaminar ligaments and related anatomic tissues already under considerable stress in response to the dynamics of discs (Steindler[2]); and, the transference of tensile (tension bar) stress from the symphysis pubis,—normally present in standing,—to the sacro-iliac and iliolumbar ligaments (Evans[3]), already overworked even in standing and walking. Furthermore, the usual position of being slumped forward tends to aggravate this situation.

That there is actually no such thing as a biomechanical perfection of the seated posture is shown further by the dynamic reactions of the passenger. In the disc reactions to vehicular vibrations may lead to biologic disturbances which might ultimately exert pathologic influences even greater than those imposed by grosser mechanical forces (Hirsch and Nachemson, quoted by Evans[3]). There are additional stresses of inertia due to repetitious loss and gain of gravitational balance during ordinary changes of direction and velocity of the vehicle. These responses of the body call for considerable supportive action by hip, paravertebral, and abdominal muscles, aided by the foot support and hand holds. Over long periods of time these activities undoubtedly account for fatigue and discomfort.

The high degree of biomechanical requirements of occupying the moving vehicle lifts

TABLE 1

PRE-IMPACT (estimated) SPINAL DEFECTS IN 100 CERVICAL CASES
(Number of Lesions)

Spinal Deficiency		*Drivers* Min.	Mod.	Adv.	*Passengers* Min.	Mod.	Adv.	*Total*
Arthritis,	Cervical	7	5	7	11	6	4	40
	Dorsal	5	0	1	4	0	0	10
	Total	12	5	8	15	6	4	50
*Disc disease,	Cervical		11			8		19
	Other		1			1		2
*Scoliosis,	Cervical		2			7		9
	Other		3			3		6
*Congenital,	Cervical		2			1		3
	Other		3			3		6

*No attempt made in these categories to grade the degree of morbidity.

Extraspinal physical deficiencies were absence of one eye and epilepsy, 1; advanced arthritis elbow, 1; and, Sprengel's deformity, 1.

TABLE 2

PRE-IMPACT (estimated) SPINAL DEFECTS IN 100 DORSOLUMBAR CASES
(Number of Lesions)

Spinal Deficiency		*Drivers* Min.	Mod.	Adv.	*Passengers* Min.	Mod.	Adv.	*Total*
Arthritis,	Cervical	0	1	0	1	0	0	2
	Dorsal	0	5	0	3	2	2	10
	Lumbar	7	8	0	5	4	1	25
	Sacro-iliac	6	1	1	6	3	1	18
	Total	13	13	1	15	9	4	55
*Congenital			11			8		19
Disc disease,	Lumbar		14			5		19
	Other		3			6		9
Scoliosis,	Lumbar		9			13		22
	Other		3			6		9

*No attempt to grade degree of morbidity from this point downwards.

Other spinal defects in drivers were Schmorl's nodes, 1; osteoporosis of vertebrae, 3; and other congenital anomalies, 1. Other spinal defects in passengers were osteochondritis vertebrae, 3; previous vertebral fractures, 2; and giant cell tumor of the sacro-iliac joint, 1. Extraspinal defects in drivers were healed osteomyelitis, 1; and bursitis shoulder, 1. For other passengers there were: amputated leg, 1; short lower extremity, 2; lipoma back, 1; osteoid osteoma femur, 1; peritrochanteric bursitis, 1; and, operative fusion hip, 1.

TABLE 3

PRE-IMPACT (estimated) SPINAL DEFECTS IN 50 MIXED CASES
(Number of Lesions)

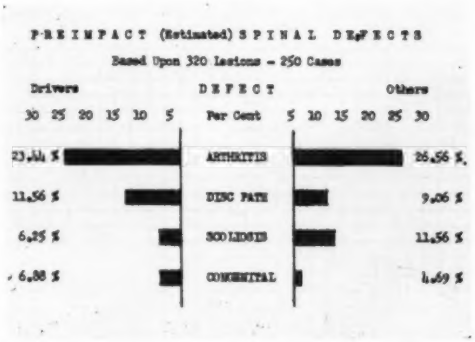
Spinal Deficiencies	*Drivers* Cerv.	Dors.	Lumb.	S.I.	*Passengers* Cerv.	Dors.	Lumb.	S.I.	*Total*
Arthritis,									
Minimal	3	2	4	4	5	2	4	0	24
Moderate	0	2	3	0	5	3	5	1	19
Advanced	2	0	2	1	2	1	3	1	12
Total	5	4	9	5	12	6	12	2	55
Congenital	2	0	4	0	1	0	2	0	9
Disc disease	0	1	7	0	3	1	5	0	17
Scoliosis	0	1	2	0	0	3	5	0	11

Extraspinal defects in one driver was acromegaly.

muscular and skeletal fitness, especially of drivers, to new levels of clinical appreciation. Tables 1, 2, and 3, accurately computed for most of the items listed but estimated for arthritis, indicate that about 80 per cent of the patients in this series suffered from varied spinal defects or deficiencies (109 drivers, 106 guest passengers).

Arthritis, the major abnormality (Fig. 1) affected the cervical spine in 60 per cent of the cases, about one-third of whom were drivers. The latter had more rear-end and angular collisions than other drivers. Since most of these collisions occurred at intersections, junctions or interchanges, where increased peripheral vision is necessary to avoid

FIG. 1



Graph is based on tables 1, 2 and 3. It is clinically significant that almost all of the items shown above, and in the tables, have a tendency toward getting worse from the standpoint of degree of morbidity. Thus, the persons with moderate to advanced arthritis were 40 years or older. It is also interesting to point out that Tanz found an ever decreasing range of motion in the lumbar spine after 35 years of age.

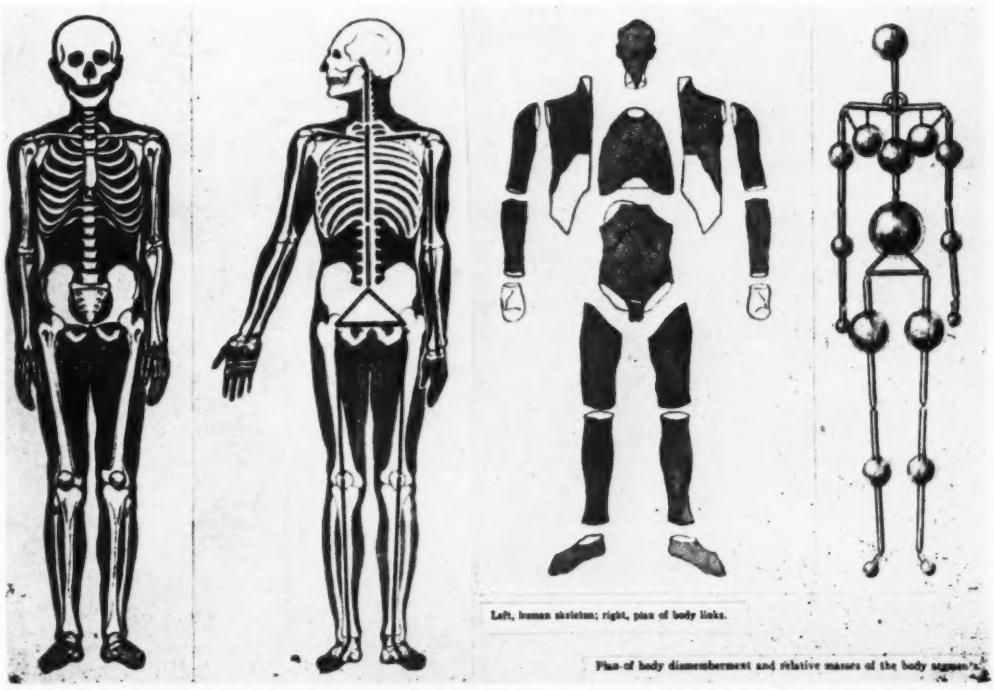
such accidents, it is assumed that possibly restricted movements of the cervical spine because of arthritis had some causal relationship to the greater-than-average (or chance) incidence in this regard. This probability was further tested by equating the total number of cervical abnormalities with types of accidents. Drivers in this latter category had more than twice as many rear-end and angular collisions than normal drivers. This distinction did not appear relative to spinal defects in the dorsal, lumbar, or sacro-iliac regions.

The connection between spinal physical defects and *predisposition to crash injury* is much more convincingly demonstrated, for example, by compression fractures of the vertebral bodies due to osteoporosis. Since the spine functions as a curved spring, it is likely that the physical defects already listed above tend to diminish this elasticity and increase the vulnerability to mechanical injury.

Impact Situation

The types of accidents are shown in table 4 and figure 2. About 80 per cent were collisions, less than 45 per cent being between automobiles. Linear, more or less concentric acceleration/deceleration patterns predomi-

FIG. 2



Left. Plan of body links (skeleton is shown at the left, at the right a pattern of body links is represented by heavy black lines (Dempster, WADC Tech. Report 55-199, [July] 1955, Fig. 32, pp. 71). *Right.* Plan of body dismemberment and relative masses of the body segments, the relative volumes of these masses correspond with bodies having a density of 8.0,— between steel and brass (Dempster, Ann. New York Acad. Sc. 63:559, 1955, Fig. 7, pp. 574). By permission of W. T. Dempster.

nated. About 85 per cent of the cervical, 75 per cent of the dorsolumbar, and 90 per cent of the mixed types of injuries were due to collisions, about 15 per cent of which were contributed by commercial type vehicles.

Slightly less than half of the cervical injuries were due to rear-end impacts; angular and forward ones ranked next in order of frequency. About 25 per cent of the back injuries resulted from forward impacts with rear-end collision and "roll-overs" being next in frequency. The order of frequency for the mixed lesions were angular, "roll-over," forward and rear-end impacts. The alarming increase in rear-end and angular collisions with their resultant so-called "whip-lash" injuries has aroused special interest in this variety of disability. A more generic pathogenesis of these injuries may be derived from the concept of body linkages (Fig. 2). The complex multiple actions of the individual intervertebral joints are appreciated best (biomechanically) when studied as integrated parts of larger units or body linkages (Steindler,[2] Dye,[4] Dempster[5]). Thus the vertebral column is reduced to three chief links, i.e., the cervical, lumbar, and stiffer thoracic one. Moreover, the principles of open or closed kinetic chains may be applied in the evaluation of these injuries. Thus, the classic "whip-lashing" is an open chain reaction, while the closed one derives from contact of the head or upper torso with the interior of the vehicle or otherwise. In the latter type of injury the clinician must be especially alert to probable concussion,—spinal, cerebral, or both.

In this series of cases, approximately one-third of the injuries resulted from open chain reactions, one-third had closed chain ones, and one-third could not be classified. For information regarding the actual forces required to accelerate or decelerate the spine beyond its normal limits of elasticity, the epochal experiments of Stapp[6] must be carefully studied. He found the spine has the lowest failing point of any structure of the body when force is applied along its length, especially from the buttocks to head in the seated position (positive *g*).

TABLE 4

TYPES OF ACCIDENTS AS RELATED TO THE THREE CHIEF CLINICAL CATEGORIES
(250 Cases)

Type of Accident	*Number*	*Per Cent*	*Cervical*	*Dorso-lumbar*	*Mixed*
Rear-end collision	76	30.4	43	24	9
Forward collision	56	22.4	18	28	10
Angular collision	42	16.8	18	8	16
Roll-overs	34	13.6	8	16	10
Forcible ejection	15	6.0	3	11	1
Ran off road	13	5.2	3	6	4
Lost control	2	0.2	2	0	0
Panic braking	2	0.2	2	0	0
Unknown	10	4.0	3	7	0
Total	250	100.0	100	100	50

TABLE 5

POSITIVE AND NEGATIVE RADIOLOGIC FINDINGS RELATED TO THE SPINAL LEVELS AND THE SEATING IN THE VEHICLE
(250 Cases)

	Driver	*Front*	*Rear*	*Total No.*	*Per Cent*
Cervical,					
Radiologically negative*	28	23	9	60	60
Radiologically positive*	20	13	7	40	40
Total	48	36	16	100	100
Dorsolumbar,					
Radiologically negative	36	24	14	74	74
Radiologically positive	16	6	4	26	26
Total	52	30	18	100	100
Mixed,					
Radiologically negative	20	13	6	39	78
Radiologically positive	0	1	0	1	2
Radiologically, both	5	4	1	10	20
Total	25	18	7	50	100

*Terms *negative* and *positive* refer to the absence or presence of radiologic manifestations of skeletal injury.

Post-impact Situation

Because of the large number of variables involved in automotive crashes, it is not sur-

TABLE 6

RADIOLOGICALLY POSITIVE LESIONS (91 LESIONS)

	Cerv.	*Dorso-lumb.*	*Mixed*	*Total No.*	*Per Cent*
Rotary subluxation C 1-2*	16	0	0	16	17.6
Rotary subluxation C 1-occiput.*	3	0	0	3	3.5
Other subluxations	8	5**	4***	17	18.6
Fractures, elements	16	2	4	22	24.2
bodies (vertebrae)	5	8	4	17	18.6
Herniated disc****	1	13	2	16	17.6
Total	49	28	14	91	100
Per cent	53.8	30.8	15.4	100	

*Controversial by some observers; **sacro-iliac joints; ***cervical; ****proved by myelography, operation or both.

One vertebral body was affected in the mid-dorsal; 2, the 12th dorsal; and one, the sacrum (in an old woman who was thrown from an automobile). There was only one case of post-traumatic coccygodynia in this series; the remainder of the back cases involved the lumbar and lumbosacral-sacro-iliac regions.

TABLE 7

RADIOLOGIC FINDINGS IN 250 CASES ACCORDING TO MEDICOLEGAL CONSIDERATIONS

	*Medicolegal**		*Not Medicolegal*	
	Negative	*Positive*	*Negative*	*Positive*
Cervical	30	23	30	17
Dorsolumbar	42	21	33	4
Mixed	27	9	11	3

*Stated another way, for the medicolegal group there were 99 negative cases (57.2%) versus 53 positive cases (68.8%); for the other group this ratio was 74 negative cases (42.8%) versus 24 positive cases (31.2%).

prising that the clinical results are often obscured, sometimes even by extraspinal complications, not to mention the various accessory spinal findings. From the standpoint of diagnosis this series of cases has been reduced to two main groups, i.e., cases with positive radiologic manifestations, and those without* (Table 5). The prominence of negative radiologic findings is notable, as well as the surprising number of positive findings (Table 6). Abel[7] contends, on the basis of his experimental and clinical experiences, that improved radiologic technics will disclose many gross skeletal lesions which are being missed today through routine methods of study.

Before one dismisses the ubiquitous diagnosis of "sprain" in the radiologically negative cases it should be remembered that the tensile stresses operating to maintain the intrinsic equilibrium of the spine (disc versus interlaminar and intervertebral ligaments) definitely predispose this structure to that kind of injury, especially in the presence of spinal defects or deficiencies.

Another clinical hurdle involves medicolegal complications (Table 7). About 60 per cent of my series of cases required some type of disability rating. Oddly enough less than half of these persons were radiologically negative, those with negative findings outnumbered the positive ones 3:1 in the nonmedicolegal categories. The clinical behavior was the same in both types of cases.

Two major pitfalls to diagnosis relevant to traumatic etiology were arthritis and/or disc disease. Both of these conditions were found about 25 per cent more frequently at the first orthopedic examination than had been estimated to be the case just prior to accident. The greater the lapse of time between injury and examination the more obscure does the traumatic relationship become.

Seven patients in this series were hurt after operations for herniations of a lumbar disc, two of whom had had a spinal fusion at the time of the laminectomy. Only one of this group required a subsequent operation for extrusion of a disc; in this instance there was also found a pseudoarthrosis of the former fusion area.

*Radiologic data were from the reports of Drs. A. B. McGlothlan, Joseph L. Fisher, Randal W. Weed and associates.

Conclusions

The critical factor in spinal injury during automotive crashes of certain types seems to be the essential instability of the seated posture. The passenger needs to be stabilized through proper restraints, proper seating, and proper fixation and special arrangements of seating.

Another important factor is the pre-impact physical condition of the riders. Physicians are not yet fully aware of their responsibilities in the field of screening drivers and/or forewarning their patients regarding these hazards. The implications of this medical equivalence should be made clearer to human and automotive engineers and to lawyers, and to physicians as well. The biomechanical approach outlined in this paper should be extended to this end.

The diagnostic pitfalls should not be cause for resignation nor yet casual doubt with respect to their clinical validity. Somewhere between the extremes of clinical patterns a satisfactory diagnostic compromise can be achieved, provided the physician sticks to his clinical last and leaves the psychosomatic features to others.

As these accidents multiply the clinical spinal manifestations it becomes necessary to multiply our biomechanical knowledge of the vertebral column, whose anatomy and physiology has been developed as a compromise between intrinsic stability and extrinsic flexibility to better meet the biologic requirements of a varied mechanical environment. The burden is great but no worse than that imposed by progress in other fields of human endeavor.

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Discussion (Abstract)

Dr. Thomas M. Foley, Jr., Bethesda, Md. Most of us have a direct or at least an indirect interest in casualties resulting from this greatest cause, including the atom bomb to date, many interesting aspects of which have been described in the paper just presented.

In one of his earlier articles Dr. Kulowski tells how his interest in this subject began. At first it was because of the annoyance of being called upon as a traumatologist at many late hours, but as time went on his irritation of inconvenience changed to one of desire to improve the apparent hopeless situation by attempting to be preventative.

This is a difficult problem and one which appears hopeless. However, through work being carried on by Dr. Kulowski and others it now seems as though improvements can be gained. Attesting to this are more and more articles in the news by those directly connected with the automobile industry. One cannot help but feel that the traumatologist is the instigator of these attempts.

I am not a statistician nor a kinesologist but fortunately the excellent tables and figures are self-explanatory. These facts do stand out to me,—namely, that the conspirators are in the 21 to 45 year age group, that they are predominantly male and that the driver is the one most frequently injured as he justly deserves.

That there was such a high percentage of spinal injuries in the over-all accident rate is surprising to one who has seen a majority of other types of injuries to the musculoskeletal system percentagewise. From cursory study of 225 ejections from planes at which the force applied is 18 G's, it was estimated that apparently 5 per cent suffered back injuries of consequence. However, whether as a result of ejection or subsequent thereto was not determined.

I am unable to give statistical data on "whip-lash" injuries. However, of the many cervical syndromes seen on our orthopedic service relatively few are due to automotive trauma, suggesting that the latter is frequently a precipitating rather than a direct causative agent in the production of this condition.

Dr. Kulowski explains well the coexistence of pathologic or mechanical attributes to the problem with which one is faced in either the private patient or medicolegal field. This in no way detracts from his plea to examine thoroughly any patient with spinal injury following automotive trauma; without question the proof of nonexistent trauma remains with the physician. Too infrequently we do see this individual as an "acute" problem and are thus faced with a dilemma of recompense versus relief of symptoms.

Our policy has been to treat all injuries of this type as if they were severe, feeling that if proper preliminary treatment is provided less likelihood or justification exists for the prolongation of complaints. In this regard less importance may be given to the initial x-ray except as an adjunct, but great importance is put upon the initial examination and the response to conservative therapy. Subsequent x-ray studies may be more informative and are considered of utmost importance.

I regret the day that the "whip-lash" injury was made public, although its clinical implication was important to us. Dr. Compere gave a lecture at our hospital last year on the syndrome and within the following week I had calls from three lawyers for details, in all respects, of this condition.

The foregoing are statements which Dr. Kulowski's article has elicited and which we encounter, either as a result of delayed treatment or our own inadequate routine treatment, and are not meant to detract from the context of his thesis.

In a recent article in the Armed Forces Medical Bulletin (Volume 7, No. 10) deaths of Navy and Marine Corps personnel in government vehicles were analyzed, and it was concluded that safety belts in hard top vehicles would have prevented many serious and costly injuries.

Dr. Kulowski's article represents a great deal of investigation and his conclusions are substantiated by his observations. We all hope that there is a possibility of evolving an automobile which will be environmentally safe, though I am sure the reckless driver can find a way to make it dangerous.

His plea for more thorough examination of driver applicants is excellent, but since speed and alcoholism are probably major factors, and prohibition has been repealed, I am sure legal prophylaxis is difficult. In another recent article in the Armed Forces Medical Bulletin (Volume 7, No. 8) it was concluded that the military would be able to provide means for the development of a dynamic and increasingly effective program of highway safety which would be applicable to both military and civilian drivers. This approach was based on the premise that the largest single factor operating in this production of motor vehicle accidents is the personality of the drivers.

Dr. Kulowski deserves the praise of everyone who has arisen at 2:00 to 5:00 a.m., as well as the citizens of his community and the United States, and I am sure that if each of those present at this meeting would make a small effort to improve his local situation definite strides would be made.

CASE REPORT

Sporotrichosis Infection of the Knee Joint: Report of a Case

WILLIAM L. STEELE, M.D., *Little Rock, Ark.*

SPOROTRICHOSIS, or infection caused by *Sporotrichum schenckii*, was first described, in 1896, by Finney and Schenck, in a St. Louis iron worker who scratched his index finger on a nail. An indolent ulcer developed, accompanied later by nodules along the course of the regional lymphatics. A case reported, in 1899, by Brayton and one by Hektoen and Perkin, in 1900, followed trauma to a finger in each instance. DeBeurmann, in 1903, recognized the first case in France and later studied hundreds of cases in that country, where this disease is of great economic and practical importance. In his comprehensive report, in 1912, DeBeurmann[1] mentioned 3 cases of sporotrichotic osteoarthritis, which were not accompanied by clinical evidence to show the nature of the lesions. He felt that sporotrichotic osteoarthritis was more common than the small number of cases reported seem to indicate. He also mentioned 3 cases requiring amputation with continued progressive disease until a diagnosis was established and treatment begun. It was said that osteoperiostitis and gummatous lesions of bone had been observed, 3 resulting in spontaneous fracture. The lesions appeared almost always in the tibia. This article is recommended for its classical value.

Wolbach and associates,[2] in 1917, reported a case of acute arthritis of the knee following a puncture wound of the joint in a 10 year old boy. This was unique in that it was not part of a disseminated infection, but was not unique in its association with a cutaneous lesion at the site of the wound. The diagnosis was made by culture of the fungus, though its presence was thought at first to represent contamination. Diagnosis was confirmed by complement fixation and agglutination tests. Collins,[3] in 1947, reported disseminated infection in a patient who had a lesion of the left knee in addition to foci in the lungs, skin, spleen and liver. This infection began two months prior to his death with swelling of the knee, followed by a generalized cutaneous eruption.

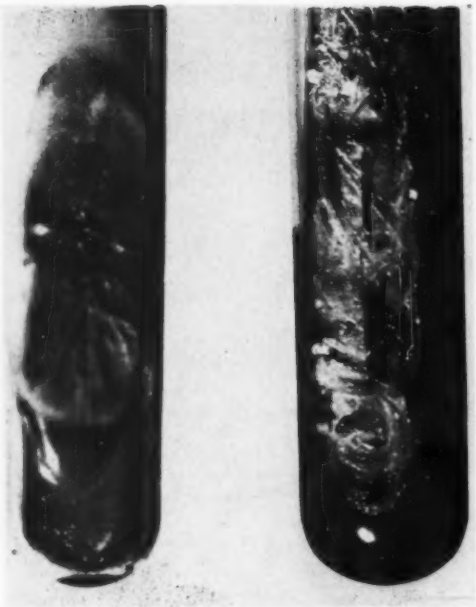
In 1954, Smith[4] also reported cases of disseminated infection with bone involvement. At that time Pipkin reported a patient who had had a skin eruption for two years when a lesion was found in the tibia and was thought to be blood borne. In 1954, from Brazil, Almeiba[5] reported 235 cases. Of these 0.9 per cent were disseminated, involving the skeleton; 0.04 per cent involved the testes, synovial membranes, bones and mucosa. The latter were felt to be an extension from the cutaneous form.

DeBeurmann[1] divided the disease into the following clinical varieties:

1. Disseminated, gummatous sporotrichosis.
2. Disseminated, subcutaneous, gummatous sporotrichosis, with ulceration.
3. Mixed forms.
4. Localized lymphangitic sporotrichosis; sporotrichotic chancre; lymphatic sporotrichosis; sporotrichotic adenitis. (This is the one most commonly described in the American literature.) The first manifestation, or initial lesion, appears at the site of inoculation, followed by ulceration and ascending lymphangitis, which is pronounced, painless and cord-like.
5. Sporotrichosis, epidermique.
6. Extracutaneous form of sporotrichosis:
   - A. Mucous membranes
   - B. Muscles
   - C. Synovial membranes
   - D. Osteoarticular
   - E. Articular

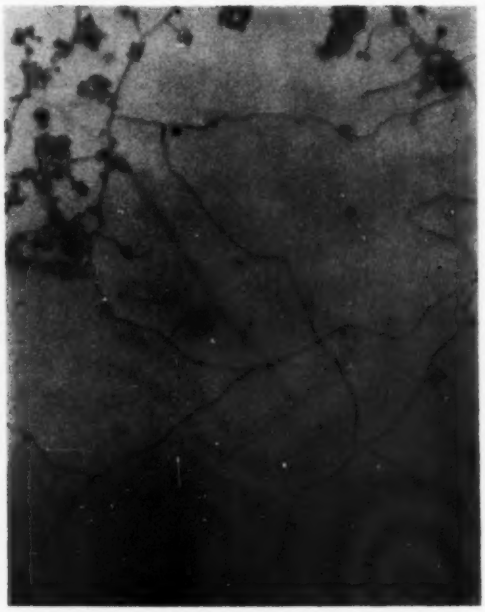
Sporotrichosis has been reported from all continents. In North America it appears more prevalent in the north central part. Sporotrichum grows in all types of soil, at a wide temperature range, and is found on

FIG. 1



Sporotrichum growing on Sabouraud's medium; growth on the left represents a mold form; that on the right represents the yeast form.

FIG. 2



Slide cultures showing "rosettes" of hyphae supporting conidiophores.

bark, thorns, wild plants, grasses, flowers, vegetables and vegetable debris. It invades man usually through the contamination of a slight wound or a puncture wound. Industrially the infection is important as shown by reports of contagion through the handling of straw in packing fragile objects,[6] the handling of fertilizer and rock wool,[7] and in florists.[6] At least 3 instances of cutaneous lesions have occurred in brick masons, presumably from contact with contaminated straw. The site of infection occurs most commonly in the upper extremities and on the side of the dominant hand. The age incidence has extended from 16 months to 71 years. It occurs most often in males; all races are susceptible. Some investigators[1,8] feel the infection probably develops in most cases because of lessened resistance in the host at the time of inoculation.

Critical examination of the cultures of Sporotrichum suggests that one species, *Sporotrichum schenckii*, is the sole etiologic agent.[9,10] Variants of the causative agent are said to exist.[1,2] Examination of purulent material from the lesion rarely reveals the fungus form; this must be remembered when attempting a diagnosis by this method. However, examination of material following animal inoculation reveals the fungus as a small gram-positive, cigar-shaped body, lying either free or within giant cells. Cultural studies are of great importance and part of the biopsy material should be planted on Sabouraud's medium. This, if kept at room temperature, will show growth of the organism in a short

FIG. 3

Yeast phase showing fusiform budding cells in culture.

period of time (Fig. 1). The colonies are at first small and white, but as the growth increases, the surface becomes thick and membranous, the color varying from cream to black. The color is not diagnostic of the species. Microscopic examination (Fig. 2) reveals delicate, branching septate hyphae, bearing conidiophores, laterally or in groups, from the ends of lateral branches. The conidiae are pyriform, ovoid to spherical, and in older cultures may become thick walled and round, being 2-4u. by 2-6u. in size. Microscopic examination of the yeast phase shows small cigar-shaped bodies which are gram-positive (Fig. 3).

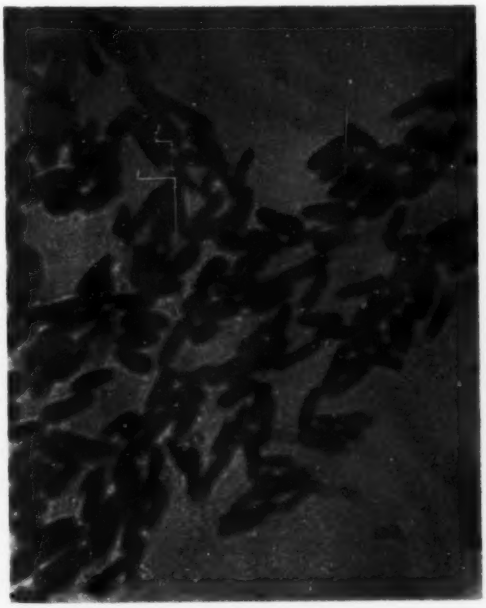
Intraperitoneal inoculation of aspirated material into experimental animals produces discrete nodular lesions, usually on the omentum, but occasionally between the coils of the intestines, on the surfaces of the liver and spleen.[9-11] Orchitis and epididymitis may occur.[2]

Intracutaneous injection of a heat killed vaccine or a polysaccharide fraction obtained from the fungus or the medium in which it was grown, produces a positive reaction within 24 to 48 hours. The skin test may become positive as early as the 5th day following infection. It is not definitely known whether the skin test remains permanently positive after infection. The serum of patients with sporotrichosis contains antibodies for the fungus; this can be demonstrated by complement fixation tests and agglutination technics.[1,2,10] Reactions in dilutions of 1:100 are considered diagnostic.[8] Preparation of the antigen is difficult and may explain the numerous cross reactions reported.

FIG. 5

Section of the sporotrichotic granuloma (X 35).

FIG. 4



Yeast phase (oil immersion).

FIG. 6

Junction of central and middle zone of lesion (X 450).

Microscopically the sporotrichotic lesion is basically a chronic granuloma, showing an amazing similarity to syhilitic, tuberculous and chronic pyogenic disease, all in one lesion. The periphery shows an intense connective tissue inflammation, with vascular dilatation, infiltration of plasma cells, connective tissue elements and lymphocytes, the latter being concentrated about the vascular structures in sheath-like formation, but also invading the collagen bundles (Fig. 5). In the midportion there are numerous large, epithelioid cells and fairly abundant giant cells of the Langerhans type, with a grouping suggestive of tubercules. Within these cell groupings are polymorphonuclear neutrophils, eosinophils, microphages and erythrocytes. These cells are especially dense near the center where there is a variable amount of necrosis and suppuration. Three zones are therefore seen: the periphery (syphiloid), the middle (tuberculoid), and the center (chronic suppurative). In syphilis the vascular changes are usually more pronounced and the epithelioid and giant cells show less grouping. Polymorphonuclear cells are less abundant and there is no suggestion of fibrous encapsulation. In tuberculosis the infiltrate is less rich in cellular elements. Necrosis is more pronounced and compact. The vascular changes are more intense and the periphery is less sharply defined.

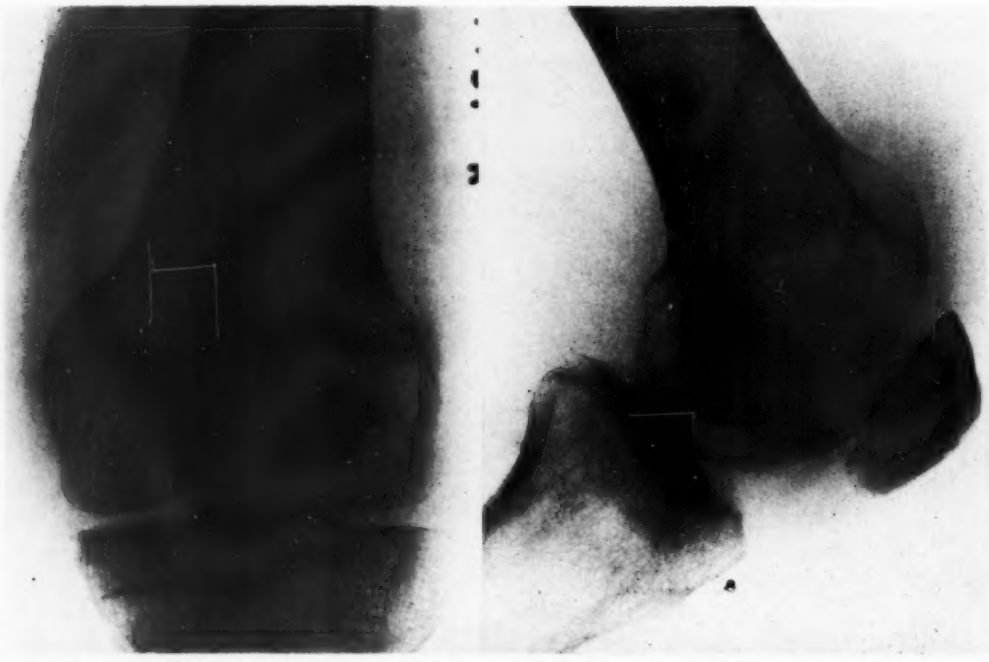
A review of the literature discloses no advance in the treatment of sporotrichosis. The saturated solution of potassium iodide continues to be the method of choice. Large doses are given three times a day and continued for 4 to 6 weeks after recovery from the lesion.

Case Report

In February, 1954, a 48 year old colored brick mason's apprentice was struck on the anterior surface of the right knee by a scaffold jack and plank.

The trauma was slight and the patient returned to his work a few minutes later without further difficulty. He did not recall any abrasion or laceration. Approximately 4 weeks later he began to have painless swelling of the right knee joint; he denied a history of local or generalized skin lesions. In about 12 weeks, in addition to the chronic swelling, he gradually began to have pain and stiffness. Initially these symptoms improved by use of the extremity, but by May, 1954, its use aggravated the symptoms. During this period he was seen by various physicians who prescribed antirheumatic therapy, which had no effect

FIG. 7



June, 1954. Showing narrowing of the joint, with thickening of the periosteum in the medial supracondylar area of the femur.

FIG. 8

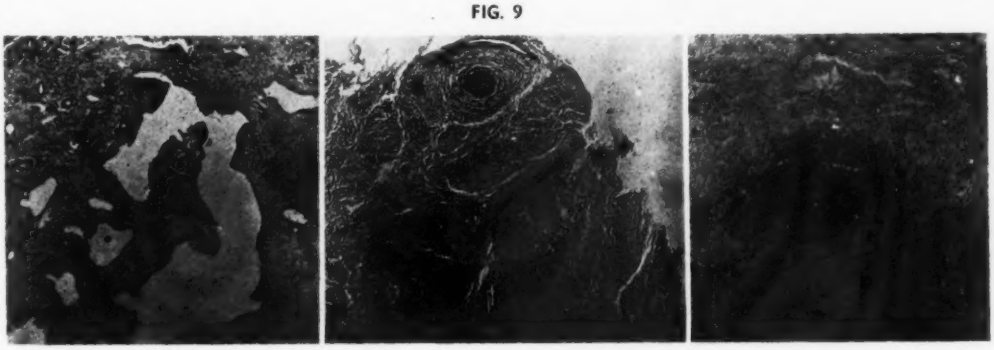
May, 1955. Showing same changes as before, with thickening and patchy areas of subchondral diminished density.

on the clinical course. By June 28, 1954, the patient was walking only with the aid of crutches, and he was seen at an outpatient clinic where aspiration of the knee was done. Thirty cc. of yellowish-red synovial fluid were obtained; culture of the fluid was negative for tuberculosis. AP and lateral roentgenograms of the right knee showed narrowing of the joint space and thickening of the periosteum in the medial supracondylar area of the femur. Areas of decreased density were noted in the subchondral femoral area (Fig. 7).

The patient was admitted to the hospital on July 8, 1954. The knee was described as being "three times enlarged, fusiform in shape, and lacking complete extension." Hgb. was 13 Gm., the white cell count 5,000, with a differential count of 10 eosinophils, 46 polymorphonuclear leukocytes, 40 lymphocytes and 4 monocytes. The urinalysis was negative.

On July 9, under spinal anesthesia, an arthrotomy was done through an anteromedial approach. The synovium was described as being 1.5 cm. thick; the joint contained approximately 15 cc. of clear yellow fluid. A pannus was said to be present and a partial

FIG. 9



A B C

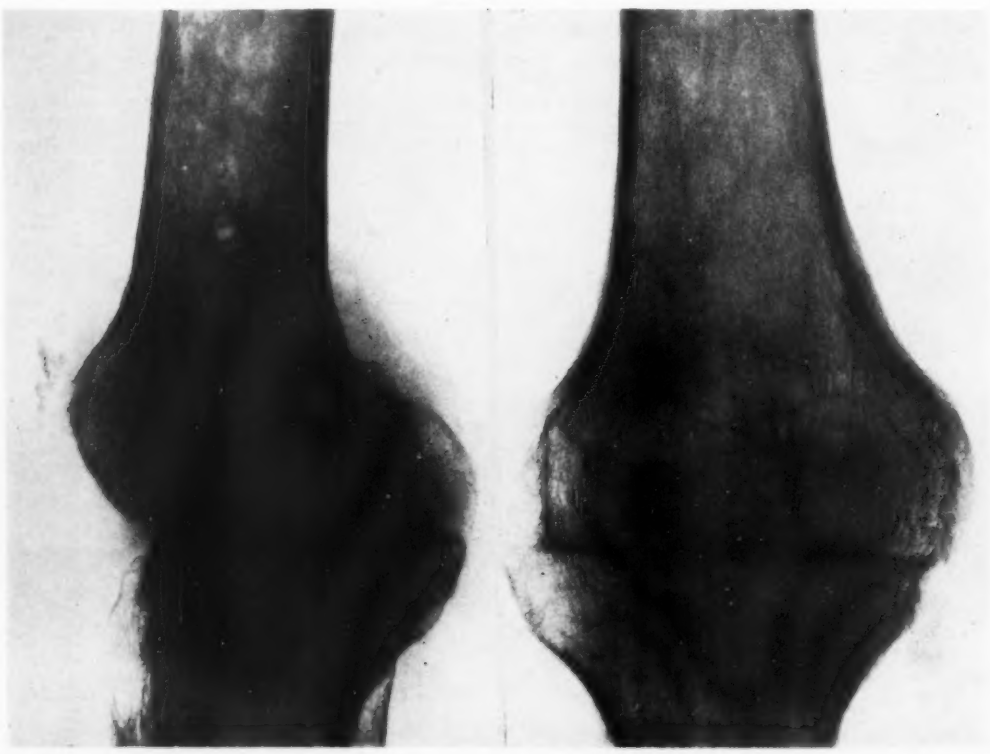
Sections at random through synovial tissues, showing the characteristic microscopic appearance of the lesion.

synovectomy was done. Sections of the synovium were described as showing chronic inflammation (Figs. 5 and 6). The postoperative course was uneventful and he was discharged on July 15. The sutures were removed July 19. (It is assumed that there was no delay of wound healing.) Motion of the knee was described on July 29 as slightly limited, but by August 30 it was considered to be "markedly limited." During this interval the patient was on exercises to develop the quadriceps, but was apparently unable to follow this program. Following his last visit the pain and swelling increased and he was forced to use crutches.

On May 27, 1955, examination revealed a thin Negro who walked with the aid of two crutches. The right lower extremity showed atrophy and the knee had a fusiform swelling, obliterating the usual landmarks. The patient had a slightly widened, well-healed operative scar along the medial parapatellar area. No skin lesions were present. The knee was slightly tender along the medial aspect of the joint margin; it was fixed in a position of 5° of valgus and 30° of flexion. There was no unusual inguinal adenopathy and the circulation was comparable in both lower extremities. Tuberculin skin tests were negative. The hemogram revealed 12 Gm. of Hgb., a hematocrit of 40 vol. % and a corrected sedimentation rate of 22 mm. at one hour; the differential count showed 11 eosinophils, 1 stab, 38 segmented cells, 48 lymphocytes and 2 monocytes. A posteroanterior roentgenogram of the chest and a skeletal x-ray survey were negative. Anteroposterior and lateral views of the right knee showed a substantial amount of soft tissue swelling, more pronounced over the anteromedial aspect of the knee. The components of the knee joint showed patchy demineralization, particularly in the subchondral area. There was a valgus deformity and thickening of the periosteum along the medial side of the supracondylar area (Fig. 8).

An exploratory arthrotomy was offered to the patient for biopsy of the tissues of the knee joint and was done on June 24, under general anesthesia. At the time of operation, beneath the quadriceps expansion was found a large mass of dense yellow-white tissue, which resembled hypertrophic scar tissue. This layer measured 2.5 cm. in thickness. The synovium was dense, thickened and reddish yellow in color. There was very little joint space present. Marked areas of subchondral erosion were seen on both articulating surfaces, the floor of these eroded areas being pink in color. Small fronds of hyperemic synovial tissue were present. Approximately 10 cc. of reddish yellow joint fluid were obtained and preserved for culture. Sections were taken from the dense tissue beneath the quadriceps expansion, the joint

FIG. 10



Postoperative roentgenogram.

lining and through the areas of subchondral erosion (Fig. 9, A, B and C). Closure was routine.

Postoperatively the patient's wound showed delayed closure; 14 days postoperatively the edges were moist, loosely coapted, and had the appearance of a 5 day old operative wound. Three weeks postoperatively the cultures on Sabouraud's media, both at 37° C. and at room temperature, revealed the fungus, *Sporotrichum schenckii* (Figs. 1-4).

The patient was given a saturated solution of potassium iodide, the initial dose being 10 drops 3 times a day. Each daily dose was increased by 5 drops until he was receiving 40 drops 3 times a day. This was continued until September 16.

On July 25 a Key-Charnley fusion was done. The knee was removed from external support on September 16 (Fig. 10).

On November 16, 1955, an intracutaneous injection of 0.1 cc. of heat killed suspension of *Sporotrichum schenckii* was done. In 48 hours at the site of injection an area of erythema one inch in diameter was present, elevated into a nodule which was red. This was surrounded by a 2 inch edematous area, projecting from the skin surface about one-eighth of an inch. This area was slightly tender to palpation and the patient complained of some itching at the site of injection. This was interpreted as being a positive reaction. Complement fixation test revealed a titer of 1:40.

Summary

1. A case of sporotrichotic infection of the knee joint is presented. It is unique since it was not associated with a cutaneous manifestation nor was there disseminated infection.

2. The industrial-economic importance of this fungus infection is a major one, since it occurs primarily in this country in agricultural or manual workers.

3. The extracutaneous manifestations of this infection make it of importance to all fields of medicine.

4. A review of the literature reveals that culture of infected material on Sabouraud's medium is essential to establish the diagnosis, since the organism is not usually found in tissue biopsies.

5. In this case there was delay in healing until iodide therapy was instituted, this method of therapy being the most efficacious for the manifestations of this disease.

930 Donaghey Bldg.

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On the Significance of Fatty Embolism as a Cause of Sudden Death in Alcoholics

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An attempt has been made to relate sudden death in the alcoholic to fat embolism from a fatty liver.

ONE OF THE RECOGNIZED TERMINATIONS of the history of prolonged alcoholism with poor dietary intake is sudden death. Among these cases there is a group in whom all that is demonstrated at autopsy is fatty infiltration of the liver.[1] These are frequently coroner's cases. Recently Durlacher and associates[2] found in 5 of 25 such cases an impressive degree of pulmonary fat embolism at autopsy. They describe a degree of embolism as great or greater than that found in post-traumatic cases. They postulate that this is the mechanism of sudden death in these heretofore cryptogenic acute deaths in chronic alcoholics.

This thesis stimulated a review of the autopsy files of the Medical College of South Carolina from 1944-1955. All patients dying suddenly with no demonstrable cause of death other than a fatty liver were selected for study. Sudden death is defined as collapse followed by death within four hours in the absence of any demonstrable disease other than chronic alcoholism. Eleven of the 14 cases meeting these criteria were coroner's cases.

Methods

Specimen bottles containing formalin preserved tissue from necropsy of each case to be investigated were obtained. Blocks of tissue were cut from the liver, kidney and three or more areas of lung. From these tissue blocks frozen sections were cut. Liver and kidney were cut at 11 micra thickness, but it was necessary to cut lung sections at 40 micra to prevent distortion of the sections when they were mounted. All sections were stained with Sudan IV, and Erlich's hematoxylin, taking particular care not to leave tissue in 70 per cent alcohol long enough to dissolve out any fat. All stained preparations were mounted with a water soluble mounting medium for preservation. In studying the stained material, significance was attributed only to intravascular sudanophilic material, with the exception of sections of liver.

Pulmonary fat embolism is graded as follows:

1+ Occasional intravascular globules on every section.

2+ Frequent intravascular globules in most low power fields.

3+ Intravascular fat in every field.

4+ Intravascular fat in every arteriole seen.

Grading of the degree of fatty infiltration of the livers is on a 4+ basis with,—1+ representing slight infiltration, 2+ moderate, 3+ severe, and 4+ massive infiltration.

Results

Fat emboli could be differentiated from other sudanophilic material by their intravascular position and tendency to conform to the lumens of the vessels. Most intravascular fat was seen in terminal arterioles and on some occasions within the capillaries.

In the sections of the lung only 2 cases showed any appreciable amount of intravascular fat (grade 2) (Fig. 1) while in only 4 cases could intravascular fat be demonstrated. Small areas of pneumonic consolidation were a frequent finding in many micro-

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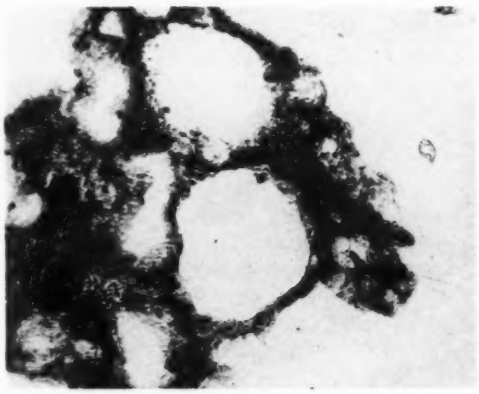
FIG. 1



Lung X 50. Intravascular fat is the dark staining material in the alveolar walls; it is present in small quantity.

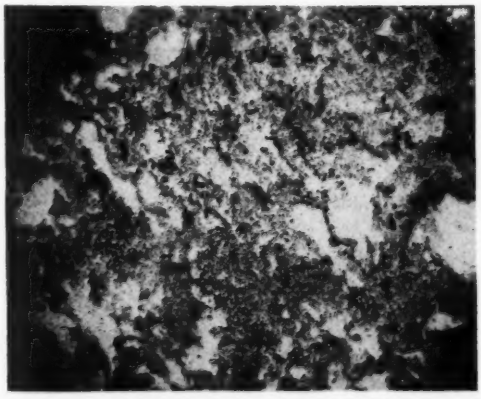
scopic fields but could not be correlated with fat embolism.

Two fracture cases with known fat embolism were arbitrarily selected for comparison. The amount of intravascular fat in the lungs of both of these cases were graded as 4+ (Fig. 2). A 4+ classification signifies far more fat than twice as much as 2+, in that every vessel demonstrable is plugged with fat.

Kidney sections were also studied; no fat emboli could be demonstrated within the glomeruli. Fatty degeneration of tubules was a frequent finding but was considered to be of no import in relation to embolism.

Liver fat ranged from 2+ to 4+, and liver weights ranged from 1,500 to 3,700 grams. In table 1 a comparison of the degree of pulmonary fat embolism is made with hepatic weights and degree of fatty infiltration.

FIG. 2



Lung X 50. Multiple globules of intravascular fat in a section from a patient dying with multiple fractures.

Discussion

Fat embolism may occur in patients with massive fatty infiltration of the liver. In none of the 14 cases studied did this phenomenon appear to be of sufficient severity to explain sudden death.

In 1929, Sebrell[3] associated a yellow liver with sudden death in dogs maintained on a blacktongue producing diet. This diet, however, was not only deficient in riboflavin and nicotinamide, but as subsequent investigations of Best[4] have shown, the lipotrophic factors as well. It might be postulated that the acute death he observed in many dogs prior to developing blacktongue was on the basis of profound fatty liver. Subsequently Sebrell[5] showed that dogs on a diet low in riboflavin developed the yellow liver and would often develop a syndrome characterized by bradycardia, cardiac arrhythmias, collapse, and coma rapidly followed by death. He found that this condition was reversed by early parenteral administration of riboflavin. These dogs had massive fatty infiltration of the liver. It is difficult to attribute the cause of death in these animals to fat embolism, because with the injection of 0.5 mg. of riboflavin massive plugging of pulmonary arterioles with fat could not be abolished completely enough to bring an animal from coma to near normal consciousness in 25 minutes. Autopsy of these dogs was remarkably similar to parallel human material. "All tissues appear entirely normal with the exception of the following: Brain-mild hyperemia of the meninges and vault. Lungs—moderate hypostatic congestion. Liver— . . . a marked yellowish mottling is present. No areas appear normal, some areas are almost a pure yellow, other mottled yellow and pink."

TABLE 1

ASSOCIATION OF DEGREE OF HEPATIC FAT AND WEIGHTS WITH PULMONARY EMBOLISM

Cases	*Pulmonary Fat Embolism*	*Liver Fat*	*Liver Weight (Gm.)*
1.	+	3+	2,220
2.	+	3+	1,900
3.	+2	4+	3,700
4.	+2	4+	1,800

Le Count and Singer[6] in 1926 discussed the possibility of fatty replacement of glycogen as a possible cause of death in patients with fatty metamorphosis of the liver. Judd and collaborators,[7] in 1934, incriminated hypoglycemia as the possible terminating factor in patients with fatty livers. Their reasoning was based on the fact that as a diabetic becomes cirrhotic the blood glucose gradually decreases. They also described spontaneous hypoglycemia in cases with hepatoma and metastatic carcinoma of the liver. Unfortunately in none of the cases mentioned in this study was a blood sugar available at the time of death. In 10 of the cases the patient was dead on arrival, most of whom had been dead several hours.

Five cases of sudden death in young adults with fatty livers were described by Graham in 1944.[1] He noted that chronic alcoholism was usually prominent in the history but acute sprees did not precede the deaths. No cause of death was given, but it was postulated that a vitamin deficiency with or without hypoglycemia might be responsible. In 5 of our cases acute sprees preceded death, and in the other 9 there was no more than chronic alcoholism. In the 2 cases with significant pulmonary fat embolism blood alcohol levels at the time of death were 250 and 320 mg. per 100 cc.

Hartroft[8] induced fatty livers in rats by feeding them choline deficient diets. In these fatty livers he demonstrated the coalescence of fat distended cells to form fatty cysts and fusion of these cysts to form secondary cysts. He demonstrated the rupture of these cysts into sinusoids and biliary canaliculi and showed this hepatic fat in embolic form in the lungs, kidney, and brain. He mentioned that this same phenomenon may be of significance as a cause of sudden death in patients with alcoholic fatty livers.

Fat embolism in diabetics was first described, in 1879, by Saunders and Hamilton.[9] Kent[10] observed that fat embolism was more frequent in diabetics than in a nondiabetic control group, and that this could not be distinguished from the pulmonary fat emboli in traumatic cases. Of special interest in his work is that all diabetics with fat emboli had some fatty degeneration of the liver. Also of interest is some recent work by Hartroft's,[11] in which he showed that hepatic fat emboli in the glomeruli result in a picture nearly identical with intercapillary glomerulosclerosis.

Durlacher's[2] finding of 5 cases of massive pulmonary fat embolism in 25 autopsies on persons with alcoholic fatty livers is not supported by the findings of this study. Fat embolism does occur in some patients with fatty livers. However, this series showed only minimal embolism in contrast to Durlacher's finding of massive fat embolism. There are some differences in the material studied. Durlacher's study was done on tissue freshly obtained from necropsy and extended over just one year, whereas in this study formalin-preserved material was used, some of which was eleven years old.

With the evidence obtained thus far it is suggested that fat embolism is not a frequent cause of the sudden death in patients with fatty livers. Although it may be an important factor in the collapse of a few such cases, the answer or answers as to why patients with fatty livers die suddenly are yet to be found. Postulates such as fat embolism, spontaneous hypoglycemia, vitamin deficiency, and failure of certain enzyme systems all will require further investigation before their respective roles in the sudden death of these patients are clarified.

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Society's Responsibility for the Health of the Industrial Worker

The health of the industrial worker is of great importance to himself, industry and to the community. This is true not only from a personal viewpoint but from an economic one as well. This series of papers pleads for understanding and aid by the community and the medical profession in attaining good health standards for the industrial worker. An increasing amount of the doctor's time and energy is being directed to preventive medicine. This is to be expected with better control of the infectious diseases and an aging population. Much of this preventive medicine can be initiated by the industrial physician who, upon finding early disease, gets the patient into the family doctor's hands and later provides the follow-up by keeping the patient in a cooperative mood.

Government

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Washington, D. C.

I AM HAPPY TO BE HERE and to join with my colleagues on this panel to discuss the subject of occupational health.

During my recent tour of duty in the federal service as Assistant Secretary of Health, Education, and Welfare, I have had much to do with national health problems. Both as a federal official and during my 21 years with Pillsbury Mills, Inc., where I was vice-president and general counsel, I have had to deal with the special problems of occupational health. I have, I hope, gained some understanding of the profound importance to our society of maintaining, promoting, and improving the health of American workers.

This combination of experience—with government and in private industry—has reinforced a conviction of mine of some years standing; namely, the importance of the *partnership principle* in our national life. It is a principle which permeates our whole social fabric—state, local, and federal governmental units, the producers of goods and services, management in its relations with labor, research science and the healing professions—endless in its working combinations and in its permutations.

Characteristically, if not uniquely American, this partnership concept is nowhere perhaps any more important or has been any more effective than in the field of health.

All of you here I am sure would agree, for example, that our remarkable achievements in health during the first half of this century are not the accomplishment or the prerogative of any single group in our population. Many have contributed—practicing private physicians, research scientists, public health administrators, private organizations, local and state governments, the great voluntary health groups, the pharmaceutical industry, and many, many others.

Most, if not all of you, would agree, I believe, that our best and most durable hope for accelerated and effective progress toward better national health lies in the continued strengthening of this partnership of the many. Certainly this is the conviction, and it has been the practice,—of the Administration in which I have had the honor to serve.

Broadly speaking, this is the role of the federal government as I see it,—a role which seeks to provide leadership without domination and assistance without undue and unnecessary interference.

With this principle in mind and with the mutual objective of working toward better occupational health, what are some of our present mutual problems? To what areas should our partnership turn its attention?

In a recent address Secretary Folsom made the important point with respect to accident prevention, that when our American resources are fully mobilized the most difficult of social problems yield. He cited the remarkable strides made in the reduction of industrial accidents,—from about 43 deaths per 100,000 workers in 1937 to about 24 in 1955. Surely the energy, the imagination, and the persistence with which industry and its partners

*Panel Discussion, read before the Section on Industrial Medicine and Surgery, Southern Medical Association, Fiftieth Annual Meeting, Washington, D. C., November 12-15, 1956.

in health tackled this problem can be applied to occupational and other health hazards.

There are two hazards which are prominent and which will become more prominent unless remedial action is undertaken soon. They are air and water pollution. These environmental health hazards which constitute an increasing drain on our productivity should be of great concern to all of us.

Action has been undertaken during the past year by the federal government in strengthening the water pollution control act and in the enactment of a multimillion dollar program of grants to municipalities for building badly needed sewage treatment plants. This is an important start. But its effectiveness will be minimized if the problem does not receive the full attention and backing, in other ways, of our local communities. I cannot think of anyone with a larger stake in seeing that community action is undertaken than the private physician.

Too little is known about the causes and the means of preventing air pollution in our industrial centers. Much more research is needed. During the past year increased funds have been made available to the Public Health Service for such research. Much more, however, will remain to be done in control measures as this research progresses. Again, you, as physicians, will have an increasingly important role to play in your local communities.

More specifically, what is the situation with respect to occupational health within American industry? In general, there are still far too many plants in which workers have few or no health services. There is a critical shortage of trained personnel. Moreover, in those plants in which health programs exist there too often remain gaps and shortages in the kinds of services they provide.

The chief area of shortage, as one might expect, is in small plants. Health services, in fact, are not now available to 70 per cent of our working population in their places of employment, most of them working in small industries. This shortage is undoubtedly one of the greatest challenges with which we are faced.

To meet it will require aggressive effort by employers, and by medical societies in particular. They both should, I believe, study carefully the experience of large industries; and, in cooperation with labor and the medical, nursing and engineering professions undertake the enormous job of education and persuasion that lies ahead.

In similar fashion, medical societies and local health departments working together can do an effective job where in-plant programs already exist to bring about improvements and help to fill the gaps that exist. Who, I suggest again, is better equipped than the physician in the local community to understand the nature of these shortages and to propose how best they may be met?

What is the federal government's role? In part, as I have said, it is to provide leadership and to lend assistance. An example of this assistance may be found in a study currently underway by the Public Health Service to develop criteria of the costs and values of such services to small plants. It will be a valuable study directed at one of the stumbling blocks to progress, and I hope it will get a wide audience.

Of the three chief problems in occupational health that I have mentioned,—the absence of in-plant programs in far too many plants, the gaps and shortages in existing programs, and the shortage of personnel,—the latter is, in most ways, the most perplexing. For, obviously, to persuade an industry to develop a health program or to improve an existing one without the people to man it is an exercise in futility.

It is apparent, certainly to me, that as our population increases, as our national interest in health and healing intensifies, and as advancing scientific knowledge enlists the time and talents of more and more scientists, physicians, and other health personnel, it will become necessary substantially to step up our whole national training and educational program.

Within this past year the federal government has taken action on this front,—by increasing the training program for scientists administered by National Institutes of Health to include about 6,000 persons annually, by instituting a program for nurses to fit them for administrative posts, and by launching a program to increase the numbers of practical nurses.

This will help. The total job, however, will call for the combined efforts, the imagina-

tion, and the creative planning of all who are members of this multipartnership in health to which I have referred. May I take the liberty of commending it to you also as a problem that very much concerns you as practicing physicians.

Occupational health and the improvement of its status in the years ahead is a field that demands the best in professional statesmanship. To the degree that all of us here play our parts with energy and persistence, so will the health of the workers be improved, and the general cause of health throughout the nation be carried forward yet another step. This is our challenge and our mutual job. The federal government—your federal government—has a big and important role to play. As is proper in a democratic society, that role will, in the long run, be shaped and altered at the will of the people. Both as physicians and as citizens it is your duty and challenging opportunity to have a hand in determining the shape and direction of that effort.

Medicine

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MY SUBJECT IS "The Community's Responsibility for the Health of the Industrial Worker." This title carries the implication that the community has such a responsibility. Some will agree it has, others will claim it has not. Both sides will support their assertions with plausible arguments. The "pros" are likely to quote the World Health Organization's pronouncement that "health" means the physical, mental, and *social* well-being of the individual. They emphasize the "social." The "antis" rely on the basic right of the individual to live his own life. They are the individualists.

The extreme on the one side is the complete welfare state; on the other it is almost the "survival of the fittest." We have come a long way from the last mentioned extreme, and it is to be hoped that we are still a long way from the first. Obviously, between these extremes the gap is wide. By the same token the subject assigned to me is big—too big to be encompassed in a single paper. It is one of those subjects in whose discussion emotion argues with logic. I shall attempt a brief comment, without too much of either.

The *Community* as a self-governing unit has its roots deep in history. From time immemorial the progress of civilization has been measurable in terms of the ability of the individual to adapt himself to the disciplines of living with other individuals. The sociologist who studies the forms, institutions, and functions of human groups, finds these disciplines universally manifest in some kind of regulatory principles. The tribe had its customs; the sect, its rules; the village, its primitive code. As the groups enlarged and merged, the regulatory principles gradually acquired the status of laws. Towns and cities set up governments; areas embracing them formed into states; states united to become nations. Always the small unit preserved its unity, and with it certain of the fundamentals of its traditional self-rule. We are the beneficiaries of that preservation.

One of the fundamentals of this self-rule—developed and seasoned through the centuries—came to this country with the earliest settlers. This was the common-law principle that the community has the power to safeguard "the comfort, health, safety, and morals" of its people. Constitutions and statutes recognize this power; legislatures and Congresses treat it with respect. One name by which it is known is "the police power." Acquaintance with your own local government will show you how basic and fundamental this power is, and how paramount it can become under the required circumstances. The imposition of quarantine is an example. But, to an audience of physicians, I need not enlarge upon that.

The foregoing is by way of preface to the statement that this *power* is for *all the people* of the community. It contemplates no preference for one group over another, and it knows no distinctions of class or kind. This is equally true of the *responsibility* that goes with the power. On the basis of the law from which it is derived, *this responsibility is no greater, and no less, for the industrial worker than for all other community members.*

Everyone is familiar with expressions of this responsibility. Milk inspection, water purification, the isolation of contagion, sanitary requirements, pest controls, immuniza-

tions—these health measures and others of the kind are so common in the daily life of the average community that they are taken for granted. The constant effort is to eliminate or control everything that is, or may become, a menace to the health of the community. This means the health of *all*. Equally, it means the health of *any*—insofar as a condition may exist or arise that will be a menace to *any*. And here is where the industrial worker comes in.

But *Who* is the industrial worker?

Obviously he is anyone who works in industry.

But what is industry?

Here we get into difficulty. Industry seems to have many definitions. To some it embraces whatever is done by all who, through their work, earn an income. I once heard an advocate of this definition asked if he thought ministers of the Gospel or school teachers were in industry. He did not answer. There is also the opinion that industrial employment embraces everyone who is under workmen's compensation. Another definition limits industry to all kinds of work except agriculture, domestic service, mining, forestry, and fishing. Some consider industry only as manufacturing. They would not include banks, stores, hotels, and the like in their definition. Still others think of industry as big business,—assembly lines and automation, factories, foundries, mills, refineries, and power houses.

Our subject suggests that the industry we are talking about will probably best fit the latter definition, and that the industrial worker, therefore, is one who works in a plant of some kind.

If we accept that, then what is the community responsibility to him? Is it to see that he works under proper conditions as to personal safety; that his working hours are spent in a healthful environment; that he is safeguarded against exposures to substances or processes that might be dangerous to his health? Is it that the community must have laws and regulations governing these things?

If that is what community responsibility to the industrial worker means, then practically every community which contains an enterprise big and important enough to require this kind of protection for the worker will find that all of this and more has already been provided for the worker by the management of the place where he works.

Anyone familiar with the technology of modern industry realizes that the employer has a considerable investment in each one of his employees. The average cost of the physical environment and facilities necessary for each job is now in the neighborhood of $10,000, and the investment in hiring and training of the worker to fill each job runs into a substantial figure. In the main, therefore, the health of the industrial worker is of much more importance to his employer than it is to the community in which he lives. It has often been said that the best way to stay well is to get a job in a plant that has a good Medical Department.

This is so true that there are many communities in which those who are officially charged with the community responsibility for the health of the people in general, could learn a great deal from the industrial physicians of the plants situated within their boundaries. Without further elaboration, I suggest that *if the average community expressed its responsibility for the health of its people in general, as completely and carefully as the average industry looks after the well-being of its employees, the health of the whole population would be vastly improved.* Almost every community has its traffic laws, smoke ordinances, sanitary regulations, requirements for the examination of food handlers and dispensers, methods of garbage disposal and sewage treatment, and standards for the condition of its streets and alleys and places of assembly. You are familiar with all these. But I dare say you also are familiar—often too familiar—with the effects of their neglect or inadequate enforcement.

To a certain extent all these things are everybody's business. Being such they suffer because often they seem equally to be nobody's business. But when the industrial physician appears on the scene, he *makes* them *his* business. He is concerned with the health and well-being of the worker inside the work-place and equally with the health and well-being of the worker outside the work-place. He has the right and the duty to be so concerned, because the one reflects upon the other, and both reflect upon the community economics. An effective illustration of this lies in the fact that the time lost by workers

from nonindustrial causes is vastly greater than the time lost from causes related to the job.

As an example, a typical situation may be cited, fully as representative now as it was 15 years ago when the figures were compiled. Out of 919 days of absence per year per 1,000 *men* workers, only 22 were related to conditions at the places of work, while 897 were from nonindustrial sicknesses and injuries. The proportion is better than 40 to one. And out of 1,851 days of absence per year per 1,000 *women* workers, only four and a half were from causes due to their work, while 1,846 were from nonindustrial sicknesses and injuries. Here the proportion is more than 400 to one.

Among the figures of the study cited are several that merit special attention. First, are the number and causes of injuries. The men have about twice as many injuries from nonindustrial causes as from industrial causes, and the women about four times as many. This ratio is important from the community standpoint, particularly in view of the practical certainty that if the figures for the nonindustrial injuries that occurred yesterday could be available they would show that the large majority were the results of traffic accidents. Second, are the numbers and kinds of sicknesses! About five-eighths of the sicknesses among men, and half of those among women are from respiratory diseases. What is the relation of these respiratory diseases to the smoke nuisance, the smog, the saturation of the atmosphere with fumes from incinerators and automobile exhausts, and the other agents that are being studied for their possible contributions to the growing incidence of lung cancer? That relation, whatever it may be, is not an industrial problem. It is a community problem. So, also, is the problem of traffic accidents.

Another example along this line is found in the 33rd Annual Report of the British Empire Cancer Campaign, for 1955. Among the findings in this Report is an interesting one concerning people who *do not* smoke tobacco. The ratio between the death rates of urban as contrasted with rural nonsmokers is about nine to one. This corresponds with the ratio between the concentrations of 3:4-benzpyrene, certain other polycyclic hydrocarbons, and sulphur dioxide, found in the air of the city, and the concentrations found in rural situations.

I have merely hinted at some of the things involved in my subject. There is not time to do more than hint.

The last hint that I want to offer is this:

Whenever a community gets to the point where it begins to think about the health of the industrial worker in terms of such things as might be called "factory inspection," then I suggest that those most directly involved in the matter do some factory inspection on their own account. If they will study the industries in their community, they will almost certainly find that the interest of the employers in the health and well-being of the workers will be both a good example and an effective reproach.

It should not be overlooked that the community responsibility for the health of the individual involves also the individual's responsibility for the health of the community. As the English poet said:

"No man is an island—every man's death diminishes me, because I am involved in mankind."

That is where I will leave you—with only the final word, that I believe the responsibility of the community for the health of its people can never be more than the sum total of the responsibility of each of its people for his own personal health and well-being.

Industry

MR. JOHN B. VEACH
President, Hardwood Corporation of America, Asheville, N. C.

INDUSTRY ALWAYS PAYS for the illness of a worker. Either the wages paid must be high enough to allow the worker to arrange all of the details himself and pay for them, or industry must provide for a large share of the details and pay the cost.

In recent years the feeling that a modern in-plant medical program is the best way has been growing very rapidly among our industrial leadership. Practically every large industry today has some type of in-plant medical program and feels some degree of responsibility for the over-all health of their workers. Much remains to be done in this field, but the big field for the future growth of this

program lies with the smaller companies. Ninety per cent of the industries in this country have less than 500 employees which is the recognized economic minimum for a full-time nurse. Fifteen years ago very few of these small companies had a group Life, Health and Accident Insurance Program,—today nearly all have it. The greatly increased cost of this insurance, plus that of Workmen's Compensation Insurance, is stimulating small industry to think of a Modern In-Plant Medical Program. There are great rewards today to any plant that can help prevent illness, disease and absenteeism.

What is the scope of a Modern In-Plant Medical Program for a small company? Our plant at Asheville, N. C., employs 170, so perhaps it would be well to tell you just what we do and how we do it.

Our program was installed four years ago by a local medical group. Under their supervision we built a small dispensary and furnished it with money from our employees' (Coca-Cola) welfare fund so that they would feel that they had a part in it. They furnish the following services and bill us monthly based on the number of employees.

The first two items are compulsory, everything else is voluntary:

1. Every new employee must have a complete preemployment medical examination.

2. Every employee who has been absent because of illness for more than 2 weeks must have a physical examination before he can return to work.

3. The dispensary is open from 1:30 to 3:30 p.m. each day with a trained nurse in attendance.

4. A doctor is in attendance two days each week with the nurse.

5. A podiatrist one day per month.

6. Periodic eye testing for machine men and a campaign for proper glasses.

7. Tetanus and "flu shots" are made available on a voluntary basis.

8. A complete record is made of all visits to the dispensary and special attention given to chronic visitors.

9. Two years ago a simple physical examination was given on a voluntary basis to 107 employees.

10. Last week, 149 signed up for a more complete physical examination which will be given at the plant in a special trailer built for this type of job. These examinations will be given on company time and are estimated to take about one hour.

Now what are the advantages to our company from this service:

1. Minor injuries are promptly cared for and many prevented from becoming major.

2. Major injuries are checked each day; the cost of dressings is greatly reduced; with no loss of time or taxi fares to go to the hospital, clinic or individual doctor's office.

3. The plant nurse also cuts the time lost by giving emergency treatment for nonoccupational conditions, such as headaches, upset stomachs, colds and the like. This permits the employees to continue a productive day and prevents many conditions from becoming disabling.

4. Consultation with nurse and doctor about personal and family problems reduces part-time absenteeism.

5. This also reduces over-all absenteeism because plant foremen also check very carefully with the nurse for the reason for each absenteeism.

6. Examination of the doctor's certificate and the employee after absence of two weeks has prevented many employees from going back on a strenuous job before they were ready.

7. Plant supervisors give much more attention to fitting the worker to his job.

8. Attention to plant working conditions, safety, sanitation and noise is stepped-up greatly under the stimulus from the doctor and nurse. The doctor makes an inspection trip around the plant each week to help in safety and sanitation.

9. The right kind of nurse or doctor can become the confidant of the employee who has emotional problems, particularly at home, and can do much to help solve them.

10. Last, and really most important of all, has been the effect of the program on the thinking of our employees. Most of them are suspicious of doctors and nurses and, at the beginning, suspicious of the motives behind the company's installation of this free program. But astute handling of the situation by our doctor and nurse in their contacts with the employees has completely overcome this situation and they are now the friend and confidant of practically every employee. Under their guidance each employee realizes more and more the importance of his own health and cleanliness, as well as that of his fellow-employees, and the importance of improved working conditions, safety and sanitation. The realization of this importance has given him a dignity that he has never thought of before,—he is becoming an entity unto himself and is beginning to recognize the importance of his health to his family, to his employer and to his associates. He is also beginning to realize that he is a part of society and as such that he has a responsibility to his community and his fellow-workers. Above all he is beginning to take more pride in his work and in his company.

What are the problems faced by small industry in trying to set up such an In-Plant Medical Program?

1. The complete lack of understanding of such a program by the average medical practitioner; his fear of it as a competitor, rather than a tool of assistance. He does not realize how closely the in-plant nurse and doctor work with the family physician and surgeon, not only in getting the employee to them at the earliest possible moment, but in keeping check on the employee after he returns to the plant. And be-

cause he will not go to an individual to talk preventive medicine, he fears, because of these ethics, to explain to the owner of a small plant what he should do and how he should do it.

2. The difficulty of getting four or five small plants to work together in hiring a trained industrial nurse and doctor. The plants, themselves, have to be sold on the advantages of such a program and if they should get together for a start, where do they find the trained personnel? It is my opinion that the leadership for such a program must come from the medical profession itself, and that it must recognize its responsibility. An alternate, of course, is the leadership of the insurance company with its staff trained not only in industrial problems, but also with the new concept of the in-plant medical program.

It is my fervent hope that the medical profession will recognize this challenge and its obligation, that it will furnish personnel trained for the job and that it will adopt a standard of industrial ethics and go to small industry and tell it what it can do.

HOTEL RESERVATION APPLICATION FORM

FOR 52nd ANNUAL SESSION

NEW ORLEANS, NOVEMBER 3-6, 1958

APPEARS IN THIS ISSUE

MAKE YOUR RESERVATION EARLY!

Medical Expense Benefit Plans*

MR. JAMES M. GILLEN,† *Detroit, Mich.*

THANK YOU, MR. CHAIRMAN. It is a real honor and a privilege to be the speaker at your luncheon today. In considering what I might say to you—what information about our business I might put before you—I realized that for a great many reasons the flow of ideas and information today should really be in the other direction.

As I think of some of the problems we face in the design of better benefit plans to cover medical expenses, I am impressed with the wealth of experience of medical groups such as this distinguished audience, upon which we can draw in the solution of many of these problems. That is why I feel it would be immeasurably helpful if we could somehow reverse positions today so that I could sit and listen to you. Since we cannot arrange that, I would like to do the next best thing; that is, to take the time allotted to me to raise with you a few of the questions and problems we are encountering currently in the employee benefit plan field. Let me preface my comments by telling you briefly about our General Motors employee benefit plan set-up.

First, for our employees and their families we have made available a wide variety of group benefit plans to help protect them in case of loss of income because of death, temporary disability, permanent disability, old age, and also against medical expenses. These plans are available on a private, voluntary basis. Except for the Blue Cross and Blue Shield coverages, our plans have been designed by General Motors specifically to meet the needs of our employees.

Second, General Motors pays the entire cost of many of these plans and shares the cost with the employee in paying for others.

Third, hospital and medical expense coverage under the General Motors Insurance Program is provided in most areas through the local Blue Cross and Blue Shield plans. Consequently, the exact form of the coverage depends upon where the employee works. In the case of employees represented by unions, coverage for each locality is agreed upon by ourselves and the unions, taking into account the needs in that community, local medical practice and the general standards set up in our insurance agreement with the unions. I might add here parenthetically that down through the years we have avoided becoming a party to any arrangement which was aimed at regimenting the doctors in any area or that attempted to fix doctors' fees.

Fourth, the comprehensive General Motors employee benefit plans in effect today have been the result of an evolutionary development which has taken place over the past three decades. It started with our first formal group life insurance plan which went into effect December 1, 1926. Since the start in 1926 we found many times that the plans or plan features we required were not being offered ready-made by insurance companies and others—they were not to be found among plans of other employers. To get the coverage we needed, we have had to take a fundamental engineering type of approach in designing our plans. We have had to design and to pioneer provisions specifically to meet the requirements of General Motors men and women. Over the years many of the plans and features we have developed have been adopted in whole or in part by many other employers. For this reason we have been, and will continue to be, projected into the social, economic and professional considerations involved in employee benefit plans to a greater extent than if we were solely concerned with selecting, cafeteria-style, a combination of ready-made plans.

With this brief background information, let me now turn to a consideration of one of the problem areas which especially concerns us at present. I refer to the need for and the desirability of providing benefits to help our employees meet the costs of illness in their families. I am sure it is also the area which

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is of most current interest to you, and the one in which your help can be particularly significant.

When an employer and his employees—or the employees through the union representing them—join to establish some kind of program as protection against the costs of medical care, they do so in recognition of a number of things:

First, they must recognize that whatever money the employer may contribute to the program is limited to money that he might otherwise spend for wages or other employee benefits such as pensions, life insurance and the like. Thus, there is a practical cost limitation.

Next, they should recognize that neither the employer, employees, unions nor insurance companies can provide the desired medical services. Only physicians and hospitals, aided by nurses and technicians, can do that. Hence, the program can only be a financing and administrative mechanism—not a means of furnishing the services.

The employer and employees must recognize also that the medical expense area of employee benefits is relatively new. It is much more difficult to predict the probable claim cost under a medical expense plan than, for example, under a group life insurance plan. Administration is not only more difficult in the medical expense area, but the technics employed are not as fully developed as in other benefit plan areas. This lag in development of administrative know-how can impose practical limitations on the kinds of protection which may be offered.

And finally there must be recognition that the program must be acceptable to employees. Sometimes it is necessary to wait until the merits of a new design approach can be understood and accepted by employees who may be accustomed to something different.

Now let us proceed within that framework. At some point an estimate must be made as to whether the desired protection can be provided within the practical cost limitation. Assuming that it has been found that it is not practical to include *all* benefits, the question becomes, "How can the available funds be used to best advantage to provide the most necessary benefits?" A decision must also be reached regarding new benefits or features which may call for administrative know-how beyond the current stage of development. There are many other decisions which must be made before a workable program of medical expense benefits can be established.

Ultimately, however, they all boil down to one basic and important decision—a decision as to what is to be left out. This decision on what to leave out is the crux of this whole question of how best to enable the employee and his family to get necessary medical care of good quality and at a reasonable prepayment cost. I believe that the biggest challenge ahead of us lies in getting a better decision as to what is to be *in* the medical expense benefit package and what is to be *left out.*

Of course, the basic question to be answered in deciding what to leave out is where the emphasis should be in providing protection. Some types of illnesses occur infrequently but may be financially disastrous to the employee and his family. The impact of others is more general, so that while the cost per case to the individual may be small, the aggregate charge to the program is large because of the higher frequency of occurrence.

Some people are convinced that employees would rather have the many small claims covered by prepayment and take a chance on the uncovered infrequent catastrophic case happening to someone else. Others have taken the opposite viewpoint. I would like to suggest that the answer might well differ for different types of benefits.

For example, the desire to have all small claims covered has been encouraged by the conventional hospital and surgical expense plans that have developed in recent years. On the other hand, in the broader field of so-called "major medical insurance," the emphasis has been on the more catastrophic types of illnesses and expenses.

A mechanism for cutting out the smaller claims is the "deductible" provision. This calls for the employee to pay small amounts himself, including the first few dollars of larger expenses. This saves the expenses of handling such small payments, and leaves more funds available for the catastrophic types of expenses.

The inclusion of a deductible provision in a conventional hospital or surgical expense plan, with no other changes, has not proved palatable to employees. Efforts along these lines have failed because the employee was expected to risk personally the same contingent liability he has under the conventional plans, because of the exclusions and limitations common to such plans. But in addition, the employee was expected to take on the responsibility for payment of deductible amounts—all merely to save a few cents in monthly premiums. I believe that the deductible approach can have appeal to the in-

dividual under only one condition; and that is if the resultant savings in premiums are pooled and used to provide coverage the employee needs but cannot otherwise have.

One of the arguments *against* the deductible approach is that such payments, even though small, may deter the individual from seeking care promptly and thus possibly impede early detection and treatment of disease. Here we have a typical illustration of this difficult problem of deciding what to leave *out* in designing benefit plans. The conventional plans generally exclude any kind of care outside the hospital except for surgical procedures. Some few plans cover limited outpatient diagnostic services, usually with a fairly low ceiling on the total amount covered during a calendar year.

In most cases the decision to leave out coverage for outpatient services is based upon the fact that claims of this nature are usually small in amount but large in the aggregate. Furthermore, it is usually not economic to add to such claim payments sufficient investigative and other administrative expense to avoid excessive or improper use.

The problem of how to provide coverage for the cost of surgical operations is *one* illustration of the difficult choices involved in deciding what to leave out when establishing a medical expense benefit program. The usual arrangement, of course, is to establish a schedule of maximum amounts the plan will pay for the various operations.

Bearing in mind that the plan is nothing more than a financing and administrative mechanism, the mere establishment of such a schedule does not of itself assure the patient of adequate coverage of his surgeon's fee. If the surgeon charges more than the plan's maximum allowance for the operation performed, the patient must pay the difference. Thus the patient may have to assume a liability which is both unexpected and unpredictable as to amount.

As you know, various means have been employed to deal with this problem. The most common is agreement between the participating physicians and the insuring agency to the effect that payment of the allowances in the insurance schedule shall constitute the full fee—the so-called service contract. Perhaps this is the most practical solution to this problem. Yet the thing that is left out in this decision can be of critical importance —namely, the doctors who do not participate —and the income limits which apply.

This leads naturally to a consideration of broader coverage, and how it can be provided on an economical basis. Such broader coverage can include benefits to help pay expenses not covered in the conventional plans—services of physicians and registered nurses both in the hospital and at home, the cost of drugs and medicines, and many other medical services and supplies for the diagnosis, treatment, and prevention of the more serious types of illnesses.

As one way of extending coverage to these additional areas and still keeping some form of financial control, the co-insurance feature has been developed. This provides that the cost of the covered benefits shall be shared between the insurer and the employee—with the insurer paying say 75 to 90 per cent.

Co-insurance is really not a new feature. Actually, most present-day plans have such an arrangement built into them in a hidden way either because the individual must pay any part of his bill which is in excess of the plan's limits, or because certain types of expenses are excluded entirely. To the extent that the individual makes such payments, co-insurance is in operation. Co-insurance is designed to provide a brake on overenthusiastic use of what may be expensive but unnecessary and unreasonable services.

The two features of a deductible amount and co-insurance are merely a means for assuring and encouraging the proper use of medical facilities and personnel.

Largely because of the recognition that the conventional plans exclude too broad an area of medical services, Major Medical Insurance has had phenomenal growth within the past five years.

I would not want my comments to detract at all from the generally excellent protection afforded by Major Medical plans. But as a means of provoking thought, let us consider one or two of the things "left out" in the design of these plans. First, it has always seemed odd to me that when the illness is serious enough to exhaust the basic hospital and surgical expense benefits, the Major Medical plans then require the patient to pay 100 per cent of his expenses until a specified deductible amount is exceeded. An-

other odd feature of these plans is that they have fixed maxima limiting the total amount which will be paid on a given case. In other words, coverage under these plans which is supposed to take care of the catastrophic illness may stop covering when the illness becomes really catastrophic. Some people today look upon these Major Medical plans simply as the next best substitute for the comprehensive plan and regard them as an interim transitional stage in the development of medical expense plans.

I am not so naive as to believe that a deductible co-insurance scheme *per se* is the way to solve all our problems in the health insurance field. Yet when we look at the ever-mounting costs of prepayment plans today, and then look at the important areas of medical care not yet covered by those plans, we simply cannot afford to reject consideration of small deductible amounts and limited co-insurance. I am certain that here is a means of better distributing expenditures under prepayment plans so as to facilitate better and more comprehensive care.

Another facet of the problem we have been discussing which warrants comment is the so-called panel-of-doctors approach. Our experience in this regard is limited to coverage we have made available at the request of our California employees through the Kaiser Health Foundation Plan. Each employee may choose either the Kaiser Plan which gives practically complete coverage including house calls, periodic check-ups, hospitalization and surgical care through a panel of doctors; or he may choose the much more limited coverage of Blue Cross and Blue Shield but with complete freedom of choice of doctor and hospital. The interesting thing to me is that despite the broader coverage of the Kaiser Plan, presently 19 per cent of our employees in California have elected the Kaiser coverage. There are other plans of this type. They illustrate still another type of decision on what to leave out when designing and establishing a medical expense benefit plan.

I have not attempted to consider in detail the many different types of plans operating today:—the many Blue Cross and Blue Shield contracts; the great variety of insurance company plans; the major medical expense plans; the comprehensive, deductible, co-insurance plans; the Kaiser type plans; the health centers operated by labor organizations and employers. But in these plans we probably have represented just about every possible variation of this decision as to what should be left out in establishing a medical expense benefit plan. Our problem is not so much one of developing new varieties as it is one of better evaluation of some of the decisions which have been made thus far so that we might reach better decisions in the future—better decisions as to what is to be left out—decisions which must be made because of limitations imposed by cost considerations; limitations encountered because these plans cannot provide the desired medical services; limitations which result from lag in the development of administrative know-how and lag in gaining employee understanding and acceptance of a new approach. Our objective must be decisions which will better enable employees and their families to get necessary medical care of good quality and at a reasonable prepayment cost. In working toward that objective we are very mindful of the fact that only a physician can determine what is "necessary medical care" and what constitutes "good quality." So in closing I am going to repeat what I said at the beginning of my talk. The know-how and the experience of this audience and the medical profession generally can give us real help in developing better employee benefit plans.

As vital and important as medical services are to the American people, it is just as important that the American people be in a position to pay for those services. All of those interested in this matter, industry, unions, insurance companies, hospitals, and you doctors, are constantly struggling with this complex problem. Many approaches are being tried. Many valuable lessons are being learned. But this is not a simple problem which can be solved by one single plan. All will be better served—doctors, hospitals, and the patients—if experimentation and growth in this field of employee benefits continues, and if each of us recognizes that the other fellow has his problems and will make his contribution toward a better understanding of what is involved.

With your help, private, voluntary plans will continue to expand in breadth and scope so that employees and their families throughout this great country of ours will receive the best possible medical care. Nothing less is good enough.

Factors Complicating Psychotherapy on a General Hospital Ward*

BERNARD BRESSLER, M.D.,† *Durham, N. C.*

The future will undoubtedly see more and more of psychiatry practiced in the general hospital. Here is an analysis of some of the basic problems to be met and solved to assure success in the years to come.

WITH THE GRADUALLY INCREASING INTEGRATION of psychiatry into the general practice of medicine on the hospital wards, certain problems inevitably have come to the fore. One very practical issue is the following:— how to best utilize the time of the psychiatrist and the availability of the ward patient in the most effective way for psychotherapy. There are certain constant elements in psychotherapy which are rather well delineated. The practicing psychiatrist in his office, or on a psychiatric ward, plans these elements, such as limits of time and the frequency of interviews, for example, with his patient. Thus the interpersonal (patient-doctor) relationship is kept within what is considered feasible for maximum efficiency in psychotherapy. However, the problem becomes entirely different in managing the patient on the general hospital ward. Assuming that a psychiatric consultation has been requested, and there are indications for psychotherapeutic treatment, certain complications invariably arise. These factors make psychotherapy much more taxing than usual, whether in the psychiatrist's office or on the psychiatric ward, where the constant elements can be well delineated.

The complications which must be considered in working with a patient on a hospital ward, might also be described as "extracurricular resistances." These problems can be described under the following headings: (1) the attitude of the referring physician; (2) the attitude of the patient; (3) problems of ward management; (4) problems of ward procedure; (5) the element of time and availability of the patient; and (6) the problem of follow-up. In the following paragraphs these resistances will be briefly elaborated on before proceeding to some accessory area of the problem.

1. *The Attitude of the Referring Physician.* For the most part the degree to which this will interfere depends upon the motives for referral. More and more physicians are recognizing the role of emotional factors in disease, even in the most flagrant organic processes, and are quick to make an appropriate referral. However, there are many referrals because: (a) a doctor wishes to get rid of a patient; (b) is angry with the patient; (c) thinks it is the thing to do; and (d) the patient insists on it.

As an example of (a), an internist referred a patient seemingly because of "no physical findings despite certain gastrointestinal complaints." Actually, I should have been forewarned by the consultation which said, "Should the patient be treated for his psychosomatic symptoms or be given a course of therapy for amebic dysentery just in case he might have something." After seeing the patient and indicating to him that some further exploration was warranted, I called the referring physician and explained the situation; in turn, he angrily snapped back, "I'll discharge him from the hospital immediately, maybe you can keep him from showing up in my office without an appointment, and just get him off my neck." The patient was a man who was struggling with his passive-dependent feelings toward a rather strict punitive, rejecting father, and it is not too difficult to imagine the attitude of this doctor to the patient while he was in the hospital.

Not infrequently the referral is made by the physician as a way of punishing the patient. It is surprising how often a doctor will

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say, "If you are not careful I will have to send you to a psychiatrist." Once in such an instance, a surgeon pulled me aside saying, "You know his pain isn't real, you go see him, he is very frightened of state hospitals." One can imagine the difficulty in working out the meaning of the referral with such a patient and the general problem of a transference reaction to the psychiatrist.

It is no less of a problem, (c) if the doctor, "Thinks a referral is the thing to do," wherein he uses it to impress the patient and just as promptly ignores the fact of the referral. In an aside, I have inadvertently overheard a physician admit as much, saying, "I don't believe in psychiatry, but it does make a good impression on a patient." The unconscious resistance to any real empathy for a patient's needs is just as dramatic as in the overly hostile doctor.

At times (d) the patient literally forces a referral, and against his will the physician does so. A woman patient, whose gastrointestinal complaints were primarily symptomatic of an involutional process, finally forced her physician to refer her to a psychiatrist. When certain specific recommendations were made this man blithely ignored the recommendations, and continued the same medical therapy that he had instituted before.

What makes the situation so difficult and makes the situation different than in the case of the usual patient seen in the office? What difference does it make that referring physicians have such attitudes toward the patient and toward the psychiatric referral? It must be remembered that during a hospital stay the patient is exposed to contact with both physicians constantly. Either consciously or unconsciously the other physician will somehow interfere or complicate the job of a psychiatrist. The interference from the physician stems from many areas. We cannot overlook the referring physician's own "unconscious" and his fear of his own fantasies, although a discussion of this topic is out of place herein. Further, one may encroach on the individual doctor's narcissism which is a very vulnerable area, not only because of his training, but because of his position in society. It is not easy to give up one's own "magic" as a healer. In addition, many physicians are literally afraid of losing patients, and jealously guard their jurisdiction over the patient. I remember one such man who, when I mentioned that the patient needed psychotherapy, brusquely said, "Well, that's all I wanted to know, if he needs psychiatry, I can give it to him."

In considering such a situation further, the psychiatrist must be even more alert than usual to any external influence from a very important figure to the patient, i.e., his original physician. It must always be recalled that in a hospital setting the patient is much more sensitized to emotional nuances than is usual. With hospitalization a very significant rapid regression occurs in the patient, encouraged by the need for an initial enforced complete dependency. In this regression, the patient is like the child (or the pet animal at home) reacting to all sorts of nonverbal communications in a very remarkable degree. The room or the ward becomes like the home in childhood when the world was the parents, but now it is the doctors, the nurses, the attendants, etc. The doctor's attitude, since we are discussing it now, is immediately transmitted to the patient, and shows up in his approach to the psychiatrist, his attitude toward the illness, and toward the ward.

2. *The Attitude of the Patient.* Obviously, if the attitude of the patient is good and the patient has been properly prepared in the referral there is no problem. But if a patient is hospitalized with an illness which is organic, or which he expects to find is organic, and is faced instead with the notion that it is "all in his head," it is frequently startling. The subsequent reaction is complicated,—the patient may absolutely deny such an impression and refuse to see a psychiatrist. Even if the patient accepts the idea there can be a varying combination of fear, shame, anger, and disappointment in his own physician, each attitude needing to be handled in a particular manner. Frequently the most that can be done in such an area is the preparation of the patient for, "things to come." It must never be forgotten that in addition to the artificial handicap indicated, there are always present the usual resistances encountered in any psychotherapeutic relationship. In turn, the extracurricular resistances are elaborated into, and complicate the usual resistances.

Although somewhat repetitious, the question of loyalty is important to a patient. If the approaching attitude of the initial physician is still that of "organic disease," the patient can only conclude that one doctor is right and the other is wrong. This is doubly complicated if he has any established relationship of some duration with his own doctor. Needless to say this is conveniently utilized by the patient in his own unconscious resistances.

Further complicating the attitude of the patient is that with a psychiatric referral there is frequently the feeling that either the patient "is crazy," is lying, or is malingering. Unfortunatley, this is frequently nothing more than a reflection of the referring physician's own feelings. Under such circumstances the patient reacts to the referral not only as a rejection but as a punishment.

3. *The Problem of Ward Management.* The aim and scope of the general hospital ward is somewhat different from the psychiatric ward. True, both are geared to a sick patient, but here divergence occurs. Ordinarily the routines on a hospital ward are mechanized as some specific physical procedure, whether it is giving a placebo, or some kind of physiotherapy, transfusion, etc. Certainly personnel are frequently kind and sympathetic, but attention to a patient's specific problem is never clarified. There are limitations of time, the large number of patients, and frequently a concomitant shortage of personnel. In addition, personnel are selected in a comparatively mechanical way, without consideration of their attitudes to emotional problems and illness in general.

Why need this be a problem? Perhaps it can be exemplified by some very brief case material. Thus, a woman with rheumatoid arthritis, who needed to ventilate her hostility at her helplessness, was continuously cut short by a nurse who told the patient to quit acting up, and chided her unmercifully. Another woman patient who needed to prove that everyone was inconsiderate and was rejecting her, could not tolerate her medication being a moment late. It was extremely difficult to explain to the nurses and the attendants how important it was either to be on time, or to explain gently and patiently each time medication was late.

One goal is to obtain a consistent prescribed attitude to the patient, such as encouraging and accepting hostility. Inevitably one can expect some breakdown in such an attempt and one must be prepared to cope with it. Such a failure must be accepted as part of the handicap on a general ward, and one should not be caught off guard. Constant reiteration to personnel individually is of utmost value, but here again, in many nurses, interns and attendants, little can be done to alter well indoctrinated character attitudes, at least on an unconscious level.

4. *Problems of Ward Procedure.* This might be entitled, "a necessary evil." A patient who is hospitalized is necessarily under observation and expects certain procedures. Frequently such procedures become comparatively endless, especially in the face of complaints which continue, and "all tests are negative." A not too infrequent result is some minor surgery, "just to do something," even though there is no real indication for operation. One physician I know, concentrates on finding "something that no other doctor has found," and continues testing until he has found something. Another patient, who felt that things were always "shoved down his throat," complained of retching. Unfortunately, his physician put down a Levin tube, confessably, because "I don't know what else to do." Thus this patient's unconscious fantasies were propagated in the hospital.

There is another way that a test or procedure can be an irritant to the psychiatrist. Being stuck with a needle, probed, investigated, etc., has particular unconscious significance for the patient. If a patient is anxious enough, i.e., in a panic state, even the simple installation of ear drops may accentuate the panic. To be able to divert such procedures and protect the patient requires patience, firmness and sometimes straight insistence.

As a corollary to the above and certainly a part of ward management, is the whole question of bedside discussions. This is a special problem in teaching hospitals where, at the bedside, impressions about patients are bandied about indiscriminately. Once again unnecessary impetus is given to the already present anxiety and more time is needed in a supportive reassurance which properly was not germane to the usual problem.

5. *The Element of Time and Availability*

of the Patient. All too frequently a patient is in the hospital for only a certain period of time. Moreover, this period is usually determined by the referring physician. It may then be true that the psyciatric problem is not the one for which the patient will continue to remain in the hospital even if necessary, nor be willing or able to continue psychotherapy later. When such a problem arises, a great deal of skill, imagination, flexibility and, of course, a resignation to the inevitable are generally necessary attributes of the therapist's approach.

6. *The Problem of Follow-Up.* This may vary from a very simple matter to being almost impossible. One may expect many patients, "to get lost," since there are so many variables. Among the latter may be considered the attitude of the referring physician, the nature of the disease process, especially the amount of organic involvement and the psychotherapeutic success in the hospital. It requires considerable skill to "round off" a period of therapy with a patient with the expectation that therapy stops with the end of hospitalization. Not only is this frustrating therapeutically, but involves a whole new area of the psychiatrist's emotional attitude toward his patient.

As a corollary to the above complications, another factor must be taken into consideration. This too has been briefly mentioned, i.e., the kind of regression that occurs in the patient who is hospitalized. Such a regression is rapid, deep, and unconsciously justified by the patient because, in a sense, it is realistically enforced. In such circumstances there is frequently a rapid resolution of many so-called functional symptoms. On the other hand, depending on what goes on in the hospital, the simple use of the regression and dependency does not necessarily solve the patient's problem symptomatically. However, this regression can be very useful if properly taken into consideration in terms of the total approach to the patient. The extent of the regression was seen, for example, in several patients whom I followed intensively following their hospitalization. In both patients the basic fantasy was one of rebirth, and in one patient, fantasies about being incorporated inside of her mother's body.

The listing of the above problems leads to the question of the various ways of handling the resistances and the regression in the hospital. What general planning should psychiatrists do to make the best use of the time and personnel, and to promulgate the most effective help for the patient? The following possibilities are certainly obvious ones and probably many more can be added to the list. (1) Should effort be concentrated on the ward personnel, whether at the level of nurses, interns, etc., and working through them leave whatever therapeutic efforts are necessary in their hands? In such an instance the psychiatrist would stand in the background as a kind of supervising figure, not intervening. (2) Should one treat the patient directly, simply disregarding the ward, and its influence on the patient, considering it only as another kind of resistance to be added to the usual resistances one sees in a patient? Herein one might naturally simply disregard the attitude of the referring physician, the nurses, the interns and so on, and simply try to work with the patient through the patient's feelings. (3) One can also raise the question that perhaps therapy is not possible under these circumstances. Perhaps the only thing a psychiatrist can do is to prepare a patient for treatment when he leaves the hospital. Not only would this save time, but this would assure the doctor of once again having a very controlled environment for his therapeutic skills. (4) Or, is the answer to be found in what has been described essentially as "goal directed therapy?" I might immediately indicate here that the terms "goal directive therapy" is a very broad, all inclusive kind of term. Such therapy would mean that we would have psychiatrists who would be very well trained to be able very quickly to isolate a patient's problem and generally know (presented with a particular aggregate of physical pictures) how to approach a problem quickly. In association with this, such a therapist would have to learn to utilize what I call "sore thumb" material, i.e., emotional content which on one level is seemingly unrelated to the patient's specific physical disease, and yet has tremendous meaning to the patient at the particular moment. As an example of what a symptom means to a patient, it may vary from a wish to get love as a defense against a psychosis, may be an escape from the responsibilities and difficulties of life, it may be a way of dominating, controll-

ing or punishing others, or it may be a way of self-punishment.

It seems to me too, inevitably, that consideration of the whole problem leads to a fairly specific proposition, or perhaps a question about the proposition. Should we, or should we not, with the tremendous accumulation of psychiatric knowledge over the years, be able to develop a definite specific psychiatric technic for use on general hospital wards? This technic would have to be proven to be as clear cut and as acceptable to the general physician, as is the usual surgical and medical technic. For example, what physician would draw blood with a contaminated syringe? What physician would operate without properly "prepping" a patient? The equivalent technic that psychiatry might develop would have to be as routine and as integrated into the total education of the doctor as are these various other procedures. The elements of the technic would have to be not only a series of "don'ts," but as much a series of "do's," which the general physician clearly understands. For example, should it not be part of the gynecologist's technic that he not take a sexual history while doing a pelvic examination? Should it not be part of the general physician's approach to the patient that all illnesses are accepted as real, and that no patient be told "it is all in your head?" What should be the constituent parts of our psychiatric technic,—assuming that we are to develop such a technic?

The schematic view of this problem is presented only to raise pertinent questions for a future solution. The whole area is a challenge which must be met, but not by "ivory tower" attitudes. Psychotherapy, with a varied associated technic, is a many sided affair from the patient seen once to the patient who undergoes the rigors of psychoanalysis. Too often it has been comfortable for the psychiatrist to isolate himself in his office and insist that only in this way is therapy possible, and writing on a chart, "the patient needs to be analyzed." Certainly this is true of certain patients, but the vast majority of needs must be met in a much less rigid manner, even in the face of what, to the psychiatrist, seems to be unnecessary artificial resistances.

EDITORIALS

EXFOLIATIVE CYTOLOGY OF THE URINE

The only means by which cancer can be positively diagnosed is by histologic study of a specimen removed by either biopsy or surgical excision. However, malignant lesions may exist for many months before symptoms become manifest, or detection is accomplished by histologic examination. In such instances the application of methods of cure may be all too late. Because of the successful application of cytologic technic in cancer of the cervix and uterus, hopeful attention has been diverted to the study of the sediment in the urine.

The case reported by Foot and Papanicolaou[1] exemplified early diagnosis although the x-ray studies of the kidney were normal. Three consecutive examinations of the sediment of the urine obtained directly from the kidney were positive for desquamated carcinoma cells; the removed kidney was grossly normal on bisection. Microscopic study of four calyces disclosed carcinoma *in situ* without invasion of the stroma in three of them. Chute and Williams[2] reported a patient in whom there were three positive smears of the urine sediment before carcinoma of the bladder was finally diagnosed at the eighth cystoscopy and the second biopsy. Also included in their report was a patient in whom positive smears of both the urine and prostatic secretion were shown, but in whom both needle biopsy and "open" prostatic biopsy were negative, and yet after perineal prostatectomy a grade III adenocarcinoma of the prostate was diagnosed. Schmidlapp and Marshall[3] reported a case wherein the first indication that cancer was present was the finding of malignant cells in the urine. Cystoscopic search failed to identify any tumor, but on suprapubic exploration cancer was found inside a diverticulum of the bladder.

Investigators, working independently, have reported varied success in the accuracy of diagnosis by this method when malignancy was present. Parenchymal and pelvic lesions of the kidney were attended by positive results in 88 per cent in one series and 50 per cent in another. In the bladder positive findings were reported in 96 per cent by one group and in 65 per cent by another in the presence of cancer; the positive results in prostatic cancer range from 83 per cent to 42 per cent respectively. In Silberblatt's[4] study of 494 patients accurate interpretation was attained in 98 per cent when no malignancy existed, 81 per cent being correct when cancer was present. This wide divergence in results may be attributed to methods of collection, number of specimens examined from each individual, the training of the pathologist and the time spent for each examination. Furthermore, those inclined toward caution will be reluctant to make an unequivocal diagnosis of such a serious disease as cancer based on study of a few individual cells. Nevertheless, under optimum conditions, the statistics suggesting a moderately high percentage of accuracy indicate that the method has merit and promises to be powerful adjunct in diagnosis. When the urine is positive the clinician is alerted to search repeatedly and in greater detail for a diagnosis, using every existing means available. A positive report must be accepted with interest, respect and caution, and be regarded as an additional but not the only factor in the complete diagnostic evaluation.

The cytologic method has been sufficiently tried to be established as an acceptable item of help. More studies, greater refinements in technic, enthusiastic cooperation and intensified training of the pathologist should stabilize the method so the laboratory of every hospital of moderate size might offer this distinctive aid toward early diagnosis.

CHARLES RIESER, M.D.

1. Foot, N. C., and Papanicolaou, G. N.: Early Renal Carcinoma, J.A.M.A. 139:356, 1949.
2. Chute, R., and Williams, D. W.: Experiences with Stained Smears of Cells Exfoliated in the Urine in the Diagnosis of Cancer in the Genito-Urinary Tract: A Preliminary Report, J. Urol. 59:612, 1948.
3. Schmidlapp, C. J., and Marshall, V. F.: The Diagnostic Value of Urinary Sediment: A Review Based on the Papanicolaou Method, New York J. Med. 50:56, 1950.
4. Silberblatt, J. M.: Exfoliative Cytology as a Screen Test for Urinary Tract Malignancy, Bull. New York Acad. Med. 29:889, 1953.

SHORTAGE OF INTERNES

The shortage of internes is a vexing problem,—troublesome to the hospital staff, the hospital administrator, the fourth year undergraduate, and the public. There are so many facets to the problem that one wonders if it can ever be solved, and at times discussions of it become acrimonious.

There are some 14,000 approved internships for which there are available about 7,000 graduates annually,—graduates of American medical schools. In general, the positions in the university and other teaching hospitals are filled. The smaller private hospitals are successful in filling only a small number of the openings in spite of attempts to "buy" internes by high salaries, apartments for married internes and the like. It is pretty obvious, however, that few internes will be "bought," if their training experience will be inadequate in such a hospital. These hospitals eke out their shortages by importing foreign graduates who commonly are unsatisfactory.

From time to time suggestions have been made with the hope of solving the interne shortage. Usually these suggestions have strong bias. Spokesmen for private hospitals, and at times in the past for general practitioners, have said that teaching hospitals and university hospitals should do away with internships and have fourth year students act as rotating internes, thereby freeing many graduates for such positions in private hospitals. In this day of modern medicine, expanding yearly, when not enough time can be found in the curriculum to acquaint the undergraduate with new items of progress, the suggestion to do away with one fourth of the medical course is nothing short of the unthinkable. Such a suggestion means either ignorance of the problems which face the medical educator, or "spur of the moment" thinking. It seems improbable that any physician in 1957 would wish this to happen to his own son if he were studying medicine. From the hypercritical, some of whom look down their nose at internships in private hospitals, come complaints that too many hospitals have been accredited for interneship in recent years and that many such accreditations should be rescinded. There may be a modicum of truth in some of this. Most of us know of some internships in such hospitals where hands have been "bought" merely to take histories and write up examinations so there will be some semblance of record-keeping needed for hospital approval. And in some of these hospitals the other side of the contract is not fulfilled, the interne having a poor experience in learning and is not given graded responsibility, either because of a poor staff professionally, and/or complete disinterest in, or lack of ability to teach. Hospitals of this type should have no internes, but this most certainly does *not* apply to all private hospitals by any manner of means.

Recently, Berger,[1] after citing his qualifications to speak on the subject, has suggested the "re-establishment of the two year rotating interneship." (It might be questioned if "re-establishment" is the proper word since there never were any great number of such openings.) He suggests that a two year rotating interneship should be approved for hospitals of 350 beds or smaller, and that "residencies should be reserved exclusively for our larger institutions." He offers this plan to fill the vacancies now existing with the one year interneship.

Though this is an oversimplification of the problem and the answer, the suggestion merits some thought. It would eliminate the almost hopeless attempts of the smaller private hospitals, which lack staff material, outpatient facilities and teaching staff, to gain accreditation for residency training programs. The second year interne, in a good teaching program under the suggested proposal, could assume increasing responsibility and fill some of the needs for residents. The proposed two year interneship would meet, or could be fitted to meet the two year graduate program so strongly recommended by the American Academy of General Practice, though it prefers some other term than "interneship." However, it would be difficult to envisage this two year program limited only to smaller private hospitals. After all, the student who wishes experience in a teaching hospital must not be deprived of this privilege, even if it is through the medium of a two year rotating interneship.

The term "rotating" interneship brings to mind the evils of rotating for set periods through a number of disciplines. If one thought rather of a two year mixed residency,

1. Berger, Herbert: The Intern Shortage Isn't Hopeless, New York J. Med. 57:3356, 1957.

and particularly if its second year permitted flexibility in some election on the part of the young physician for work in some particular field, it might not only satisfy the American Academy of General Practice, but conceivably might even be tailored in such a way that the second year might be acceptable to certain of the specialty boards. This would then permit the "junior" resident beginning his third year to assume much responsibility. In such a scheme the "straight" interne might not be missed too much for on some services at some places he is actually a supernumerary.

This suggestion by Berger has some of the same philosophy currently expressed by the American Academy of General Practice. However, the latter quite probably and properly would not wish to accept the suggested restrictions relative to the hospitals in which the program were to be carried out. The Academy quite certainly would not wish to have its program limited to nonteaching hospitals. Nevertheless, the suggestion is of interest and permits of speculative thought.

25 YEARS AGO

Animal Experiments with Adrenal Cortical Extracts*

"Since the extraction of a potent principle from the adrenal cortex by Swingle and Pfiffner and by Hartmann much greater interest has centered upon this gland than ever before. Animal experimentation has at last acquired a tool to work with, and it is being used extensively. Great hopes have been entertained for the successful treatment of Addison's disease, and the cortical extract has been used for this purpose with some degree of success by Rowntree and others. The very nature of this condition, however, would preclude the possibility of a cure, since it is caused in most cases by a progressive, destructive lesion of the adrenal glands. The only hope therefore is that cortical extract can replace the normal secretion. This would mean lifelong treatment, ...

" . . . lesions causing hypofunction of the cortex have been associated with (1) pseudohermaphroditism in the newborn; (2) a questionable failure of development of the central nervous system in anencephaly (probably coincidental); (3) hyperplasia of the thyroid; (4) Addison's disease; (5) myasthenia gravis.

"It is these physical and sexual changes which have interested us most. The adrenal cortex is so intimately bound up with, not only the phenomenon of reproduction, but the physical configuration of the body, that these aspects seem to be of much greater biological significance (and probably, in the future, of greater practical significance) than the more dramatic, but much more rare disease called Addison's disease. We have, therefore, confined our studies to a few of the thyroid and sexual phases now susceptible of investigation. Rats were used advisedly, despite the impression that the adrenals cannot be removed completely from these animals. . . .

" . . . Following the estrus cycles of mature female white rats by vaginal smear we found that the normal sexual rhythm stopped following adrenalectomy. Autopsy findings in these animals showed a consistent and early degeneration of the corpora lutea of menstruation. It was this association that led Vincent to suggest that the corpora lutea acted as accessory adrenal cortices, and by this mechanism Stewart and Rogoff explained the longer postoperative survival period of pregnant dogs. The corpora lutea of rats are constantly present in the rat ovary as bodies of menstruation, lactation, or pregnancy. We were able to observe the same. . . .

"We have shown that a definite connection exists between adrenal insufficiency and such changes in the lymphoid apparatus as regeneration or hypertrophy of the thymus and hyperplasia of the lymphoid elements.

"In the thyroid an increase in size accompanies adrenal insufficiency. The removal of the thyroid gland extends the postoperative survival period of adrenalectomized animals. Those with adrenal insufficiency are killed by a dosage of thyroid extract which does not affect the normal animals.

"The reproductive system responds to adrenal insufficiency by: a cessation of estrus; a softening and atrophy of the testicles; abortion or resorption of the fetuses (if the insufficiency occurs before the seventeenth day of gestation); and cessation of lactation. All of these changes apparently operate through the secondary atrophy of the gonads.

"We were unable to prevent any of these changes by administering cortical extracts carrying the viable principle.

"The effect of extract in normal animals has produced a cessation of the estrus cycle of rats, and degeneration of the ovary of chickens.

"Finally, cortical extracts as made by us either contain more than one principle or else we have not extracted the complete biological unit."

*Carr, J. L., and Connor, C. L.: Animal Experiments with Adrenal Cortical Extracts, Ann. Int. Med. 6:1225, 1933.

Executive Committee Highlights

The Committee, composed of Dr. Fount Richardson, Chairman, Drs. Harry Lee Claud, George D. Wilson, Robert D. Moreton, W. Kelly West and Milford O. Rouse, held its interim sessions in Birmingham, February 1-2. Dr. J. W. Jervey, Jr., was unable to attend because of illness. Others present were Dr. R. H. Kampmeier, Editor; Mr. V. O. Foster, Executive Secretary; Mr. C. P. Loranz, Advisor and Professional Relations Counselor; and Mr. Robert F. Butts, Business Manager. Guests were representatives of Smith, Kline & French Laboratories and Charles O. Finley and Company.

Plans for New Orleans

The Committee heard reports on work already done on the meeting from the Executive Secretary and the Business Manager. From the Executive Secretary, it was learned that two organizational meetings had been held in New Orleans in December and January with state and local medical society and auxiliary officials and with local key Southern Medical Association officials headed by Councilor J. Kelly Stone and First Vice-President Edwin Hugh Lawson.

Local Committee on Arrangements

Already, the General Chairman on Arrangements, Dr. Edwin L. Zander, 3330 Canal Street, New Orleans 19, Louisiana, had been selected, and Dr. J. Kelly Stone had been named Chairman of the Executive Committee and Dr. Lucien A. LeDoux was selected Chairman of the Advisory Committee of the Committee on Arrangements. The third planning meeting, scheduled for March 3-6 in New Orleans, will see the Local Committee well organized with some 300 New Orleans physicians appointed to more than 40 separate subcommittees. The "Kick-Off Dinner Con-

DOWNTOWN NEW ORLEANS

ference" which will be attended by top SMA officers, the Local Executive and Advisory Committeemen and the chairmen of the 40-odd subcommittees, will be held in New Orleans on March 27.

Physical Facilities

Business Manager Robert F. Butts reported completion of arrangements with the Convention Bureau, local hotels, and the Municipal Auditorium. The address of our Housing Bureau, which will handle all hotel reservations, is P. O. Box 1460, New Orleans 5, Louisiana. Hotel commitments with their public space include the Roosevelt, 450 rooms; the Jung, 700 rooms; the Monteleone, 350 rooms; and the St. Charles, 200 rooms. Another 500 rooms are available in other hotels and motels including the recently remodeled New Orleans Hotel, the De Soto Hotel and the De Ville Motel. The Roosevelt and the Jung have been named co-headquarters for SMA, and the St. Charles has been selected for Auxiliary headquarters.

The Municipal Auditorium, located within three to six blocks of major hotels, will house the entire Scientific Assembly, including exhibits and color TV.

Schedule of Major Events

FRIDAY, October 31

First Session of Executive Committee and other committees of the Council.

SATURDAY, November 1

First Session of the Council.

SUNDAY, November 2

REGISTRATION—All day, Municipal Auditorium (an advance registration for all New Orleans physicians will be held at strategic locations during week of October 27-31).

MONDAY, November 3

Second Session of the Council.

Section Programs begin 9:00 a.m.

President's Luncheon—Noon.

Evening reserved for Medical Student Representatives' Dinner, Section parties, Alumni dinners.

TUESDAY, November 4

Past Councilors' Breakfast.

Sections continue, 9:00-12:00 a.m.; 2:00-5:00 p.m.

Doctors' Day Luncheon.

Evening reserved for Past Presidents' Dinner and additional Alumni, Section and Fraternity functions.

WEDNESDAY, November 5

Section Officers' Breakfast.

Sections continue.

Geriatrics Symposium.

PRESIDENT'S NIGHT—Annual Dinner, business, entertainment.

THURSDAY, November 6

Sections continue—conclude meeting at noon.

Postconvention Tour to Mexico leaving New Orleans by air Thursday afternoon—5 and 10 day tours. International Travel Service, Palmer House, 119 S. State Street, Chicago, Tour Directors.

Medical Student Representatives

This year thirteen medical schools will be invited to send an elected representative of their senior class to the meeting as Association guests. Medical schools to be represented are Tulane University, Louisiana State University, University of Mississippi, Baylor University, University of Texas, Southwestern, University of Arkansas, University of Tennessee, Vanderbilt University, University of Oklahoma, Washington University, St. Louis University, and University of Missouri. This will complete the Association's project of entertaining a senior representative of all of the medical schools in the territory.

Color TV

Arrangements have been made again this year with Smith, Kline & French Laboratories to conduct at least five color TV programs. They, as last year, will be sponsored as an official part of the Sections participating. Shows will originate at Charity Hospital and will be screened in a special TV Room in the Auditorium. Sections sponsoring will meet in the TV Room during the session when their TV program is screened. General Chairman of the Color TV Co-ordinating Committee in New Orleans is Dr. Adolph A. Flores, Jr. Each sponsoring Section Secretary will ap-

point a New Orleans Chairman of Color TV to plan and present their program, and he will be a member of Dr. Flores' Co-ordinating Committee.

Woman's Auxiliary

The Auxiliary will be headquartered at the St. Charles. Already, Mrs. C. Grenes Cole, General Chairman, and Mrs. Boni DeLaureal, Co-chairman on Auxiliary Arrangements, are well along with their plans. These talented and capable generalissimos attended the last SMA New Orleans conference and will participate along with the Auxiliary's President, Mrs. Walker L. Curtis, College Park, Georgia, in the Kick-Off Conference, March 27. Their meeting is one that no member's wife should miss. New Orleans is a natural for the ladies! —and it's not bad . . . for the gentlemen!

Proposed Committee on Scientific Assembly

A Study Committee on Scientific Assembly was created to evaluate a proposal presented by Dr. Rouse designed to improve the quality and the mechanics of the scientific work of the Association. The areas of study will include the present operations of the Sections, duties of officers, terms of office, and program planning. The Committee will evaluate the desirability of a permanent Council Committee on Scientific Assembly with the duty of overall co-ordination of the scientific program of the Association.

All SMA officers, Councilors and Section Officers attending the AMA in San Francisco in June will be invited to a luncheon conference to discuss the work, scope and objectives of the Study Committee.

Chairman Richardson appointed the following members of the Study Committee: Dr. Milford O. Rouse, Chairman, Dr. Julian Ruffin, Dr. J. Morris Reese, Dr. Lenox D. Baker, and Dr. May Owen. The Committee will make its report and recommendations to the Council at the New Orleans meeting.

Life Membership Schedule Adopted

Pursuant to action at Miami Beach, the Executive Committee approved a schedule of life membership dues and the modus operandi as follows:

1. Life membership in the Association may be voluntarily secured upon application by any member in good standing and the payment of the following amounts according to age on the date of application:

Up to and including age 50	$225
51	210
52	195
53	180
54	165
55	150
56	135
57	120
58	105
59	90
60-65	75
66 and up	50

2. Life membership dues, once paid, shall be for *life,* and life members shall not be required to pay any additional amounts, irrespective of any future increase in regular dues.
3. Life members will receive a framed certificate of their Life Membership bearing the signature of the proper officers and the seal of the Association.

Nonresident Membership

The Committee recommends to the Council the establishment of a nonresident membership in the Association available to doctors of medicine living outside the territory of the SMA who are members in good standing in their state and local societies and otherwise meet the requirements for membership in SMA. Such members would petition the SMA and be approved by three SMA members. They would pay the regular dues, receive the Journal and other publications, but could not vote nor hold office. Proper application forms will be available from the headquarters office.

Study Committee on Admission of New Mexico Appointed

Following reports of much interest among physicians in New Mexico to belong to the Association, the Committee authorized a Study Committee to investigate the matter, and Chairman Richardson named President West as Chairman of the Committee. A Study Committee on Admission of Delaware, composed of Drs. Harry M. Robinson, Jr., Harry Lee Claud, and Donald S. Daniel, is conducting similar studies. The Executive Secretary was instructed to send the Quarterly Bulletin to physicians in these states.

Report of Committee on Meeting Places

The Co-chairman, Dr. George D. Wilson, reported that Baltimore was definitely out for 1960 because of conflicts and available dates. The Committee recommended that St. Louis be the first choice for the 1960 meeting and Miami Beach second choice. The recommendation was approved and referred to Council.

Report of Insurance Committee

Dr. Robert D. Moreton announced that the Insurance Committee had had two meetings with Mr. Charles O. Finley, Administrator. He reviewed the promotion now going out on the "Big 3"—Sickness & Accident, Accidental Death & Dismemberment, and Catastrophic Hospitalization. Three hundred thousand brochures on each plan have been printed, and one mailing of each has gone to 30,000 physicians. A series of ten follow-up letters over the next ten weeks will be sent on the Hospital Program. Mr. Finley reported a very favorable claim-loss ratio on the old Sickness & Accident Program which is being retained for the members presently insured. The Executive Secretary reported that within three weeks the office had processed 744 insurance applications of which 236 were new members. The Executive Committee commended Mr. Finley for his efforts and the results of the new program. It also commended Dr. Moreton as Chairman of the Insurance Committee. The Committee reported that studies are being made on a Group Life Program which will be reported at the New Orleans meeting.

Other Capsules

1. Approved $150 honorarium in lieu of "traveling expenses" for Section guest speakers.
2. Approved the reappointment of Drs. J. F. A. McManus and Preston A. McLendon to the Editorial Board for five year terms.
3. Approved the recommendation of the Committee on Meeting Places to name St. Louis as 1960 meeting place.
4. Instructed that certificates be given medical student representatives.
5. Accepted report and recommendations of the Executive Committeee of the Home Building Finance Committee calling for specific activities designed to secure contributions to the Building Fund.

Other Committee Appointments

Chairman Richardson announced appointments to the *Selection Committee* of the Council as follow: Dr. J. Kelly Stone, Chairman, Drs. Jack C. Norris, J. W. Jervey, Jr., Harry M. Robinson, Jr., and J. Duffy Hancock. This Committee will "seek, receive, and consider nominations for all elective offices of the Association." This Committee will place the names of three nominees for each office before the Council for nomination for the offices of President-Elect, First Vice-President, and Second Vice-President.

Committee on Geriatrics Symposium—Dr. A. Clayton McCarty, Chairman, Dr. Milford O. Rouse, and Dr. R. Lomax Wells.

Committee on Admission of New Mexico—Dr. W. Kelly West, Chairman, Dr. Milford O. Rouse.

Members of the Committee visited and inspected the new headquarters building now under construction in Birmingham.

V. O. F.

WOMAN'S AUXILIARY TO THE SOUTHERN MEDICAL ASSOCIATION

Minutes of 33rd Annual Convention

Miami Beach, Florida, November 11-14, 1957

PRECONVENTION BOARD MEETING

The Preconvention Executive Board Meeting was held November 11 in the Zodiac Room of the Delano Hotel. Mrs. Oscar W. Robinson, President, greeted the guests and presented Mrs. John J. O'Connell, immediate Past-President, who gave the invocation.

Following the luncheon, the President recognized *in absentia* Mr. C. P. Loranz and Mr. V. O. Foster of the SMA headquarters office. Mrs. Robinson presented a personal gift of $100.00 to Mr. Loranz for the Building Fund of the Association in lieu of gifts to members of the Executive Board.

Other guests recognized at this time were: Mrs. V. O. Foster, representing Mr. Foster, Mrs. Paul C. Craig, President of the Woman's Auxiliary to the American Medical Association, Mrs. William P. Smith, Convention Chairman, and Mrs. John M. Dix, Publicity Chairman. Others present included seven officers, ten committee chairmen, eleven councilors, and six past-presidents. Mrs. Boni J. DeLaureal, New Orleans, President of the Woman's Auxiliary to the Louisiana State Medical Society extended an invitation to the Auxiliary to meet in New Orleans in November, 1958.

Mrs. Robinson, reporting to her last Executive Meeting, expressed her appreciation for the cooperation of all members during the year and expressed appreciation for the hospitality shown her at various state meetings throughout the South, and particularly to Mrs. William P. Smith for arranging the luncheon.

Since the minutes had been approved by the Reading Committee and published, Mrs. Maynard Emlaw moved that they not be read. The motion was seconded by Mrs. Walter A. Porter and carried.

Mrs. Walker L. Curtis, President-Elect, brought greetings, mentioning that among her various pleasant activities of the year was the privilege of representing the Auxiliary in Birmingham on August 4, 1957, at the SMA's Ground-Breaking Ceremony, and in attending the dedication of the Crawford Long Memorial in Jefferson, Georgia.

Mrs. William A. Garrott, Recording Secretary, reported that the minutes of the Postconvention Board Meeting of 1956 had been approved by the Reading Committee and published in the May issue of the *Southern Medical Journal*.

Mrs. Edwin Guidry, serving for Mrs. John D. Gleckler, Corresponding Secretary, read a number of telegrams of greetings and good wishes to the Convention. In the absence of Mrs. John C. Perry, Historian, Mrs. Shelley Davis moved that the report be filed. The motion was seconded and carried. Mrs. Garrott brought greetings from Mrs. W. W. Potter of Knoxville, Custodian of Records. There was no report.

Mrs. Thomas E. Strain, Auditing Chairman, reported that the Treasurer's books were in good order. It was moved by Mrs. James N. Brawner, Sr., that the report (Treasurer's) be given in the General Session on the 12th. The motion was seconded and carried.

In the absence of Mrs. George D. Feldner, History of Doctors' Day Chairman, Mrs. Emlaw moved that the report be filed, along with the reports of all chairmen not present. The motion was seconded and carried.

Mrs. O'Connell, acting as Chairman of the Nominating Committee in the absence of Mrs. V. Eugene Holcombe, announced that the Committee had met and would give its report at the General Meeting.

The proposed budget for 1957-1958 was presented by Mrs. O'Connell in the absence of Mrs. C. T. Shepherd, Chairman of the Budget Committee. Mrs. Howard moved that the Executive Board recommend the adoption of the budget to the General Session. The motion was seconded by Mrs. George Owen and carried.

Mrs. W. G. Thuss, Chairman of Doctors' Day Committee, presented a recommendation of the Committee that exhibits should be a separate classification and not considered in judging as part of the best Doctors' Day observance. (Explanation: Our judging is set up on the point system, and the exhibit counts 25 points. We feel that many states may have a full and excellent over-all observance that possibly could not be put into a scrapbook, yet the state has 25 points against it automatically.) The recommendation was accepted.

Mrs. J. Ullman Reaves, Chairman of the Jane Todd Crawford Memorial Committee, reported that through the able assistance of the Councilors 109 gift subscriptions to the *Southern Medical Journal* were sent to residents in gynecology. She announced that 1,500 copies of the 1957 edition of the Jane Todd Crawford brochure were on file in the headquarters office in Birmingham and will be placed in the new Auxiliary Room when completed.

Mrs. Robinson requested Mrs. Guidry to read recommendations from SMA Councilors as to the best use of the balance in the Auxiliary's Jane Todd Crawford Fund, which is now slightly more than $5,000.00. Most of the recommendations were that the money be used to furnish a room in the new SMA building with some memorial in honor of Jane Todd Crawford and Dr. McDowell. Mrs. J. U. Reaves moved that the money remaining in the Fund be used in the Auxiliary Room in the new building in Birmingham, including a large bronze plaque for the door of said room, a painting of Jane Todd Crawford, and the remainder of the Fund used in furnishing the room. Mrs. James N. Brawner seconded, and the motion carried.

Mrs. George Owen, Membership Chairman, reported an increase in membership in Kentucky, Florida, District of Columbia, Maryland, Mississippi, Tennessee, North Carolina, and South Carolina—a gain of 109 members.

Mrs. Emlaw, Memorial Chairman, reported that the use of memorial cards had seemed successful when used. She reported the death of six husbands of Auxiliary members.

Mrs. Robinson recognized Mrs. Smith, Convention Chairman, and Mrs. Dix, Publicity Chairman, thanking them for their splendid work and cooperation.

In the absence of Mrs. J. R. Horn, Jr., her report on Research and Romance of Medicine was filed.

Mrs. Emlaw moved that the use of an official emblem for Doctors' Day as suggested by North Carolina be referred to the incoming Doctors' Day Committee. The motion carried.

Mrs. Davis, Revisions Chairman, reported on proposed amendments and revisions to the Constitution. Mrs. Stover moved that all revisions be recommended for study by the incoming Executive Board, and that we recommend the preparation of a revised Constitution and By-Laws to be presented to the 1958 Convention. Mrs. Perry D. Melvin seconded and the motion carried.

At the suggestion of Mrs. Howard, Treasurer, Mrs. Emlaw moved that the Revisions Chairman, Mrs. Davis, be reimbursed in the amount of $54.00 for printing expense. The motion carried.

Mrs. Robinson extended a gracious invitation to the members to attend a cocktail party which she and Dr. Robinson and Dr. and Mrs. Curtis were hosting that evening.

(Signed) MRS. OSCAR W. ROBINSON, *President*
MRS. WILLIAM A. GARROTT, *Recording Secretary*

GENERAL SESSION

The General Session was held in the Fala Room of the Delano, November 12, 1957. The meeting was called to order by the President, Mrs. O. W. Robinson, at 9:00 a.m. The Reverend R. Wiley Scott, D.D., Minister, Miami Beach Community Church, gave the invocation.

Dr. W. Kelly West, President-Elect of the SMA, was presented. He pledged his cooperation with the Auxiliary and its activities. Dr. Milford O. Rouse, First Vice-President, brought greetings, saying that he was proud of the Association and its Auxiliary because it presents service as well as social contacts for doctors and their wives.

Dr. William C. Roberts, President of the Florida Medical Association, brought greetings and Dr. Donald F. Marion, SMA General Chairman, was presented. He told of his privilege of being a part of the 51st SMA meeting and was generous in his praise of the cooperation of the headquarters office and with the Auxiliary Chairman, Mrs. Smith.

In the address of welcome, Mrs. Perry D. Melvin, President, Woman's Auxiliary to the Florida Medical Association and SMA Auxiliary Councilor, extended most cordial greetings to the Convention and urged a return visit in the near future. Mrs. William P. Smith, President of the Woman's Auxiliary to the Dade County Medical Association also brought greetings. Mrs. W. Kelly West, Past-President, responded to the addresses of welcome stating that the guests considered it a

privilege to come to "play-land," but to try to elaborate on the advantages of this Southland would only be guilding the lily. She thanked all of the local committees for their good planning.

Following the presentation of the President-Elect, Mrs. Walker L. Curtis, Mrs. Paul Craig, President, Woman's Auxiliary to the American Medical Association was introduced. She said it was a joy for her to see the Southern in action and that she liked the projects sponsored by the Auxiliary. She said there was luster to the Southern Tradition which should brush off on other states—the tradition of balancing the past with the future. She urged members to interpret changing medical care to the public.

Mrs. Smith, Convention Chairman, introduced Mrs. Arthur Wood, Chairman of Pages. She invited the members and guests to attend the tour of Viscaya and tea on Wednesday afternoon, November 13.

The Secretary, Mrs. William A. Garrott, called the roll of officers. Those present were eight officers, nine chairmen, eleven councilors, and six past-presidents.

Mrs. Emlaw, Chairman of Memorials, reported that eleven members has passed away during the year, presenting a beautiful tribute to them while using a white rose and a lighted white candle as accessories to the memorial service.

Reports of State Councilors were heard by regions with the Vice-Presidents presenting the Councilors from their respective regions. Serving in the absence of Mrs. Harry L. Johnson, Second Vice-President, was Mrs. John M. Chenault of Alabama, along with Mrs. George Owen, First Vice-President; and Mrs. F. A. Holden, Third Vice-President.

Those present and reporting by states were:

Mrs. John M. Chenault—Alabama
Mrs. Perry D. Melvin—Florida
Mrs. John M. Brewer—South Carolina
Mrs. Roy A. Douglass—Tennessee
Mrs. Richard Dunkley—Washington, D. C.
Mrs. William Ray Moore—Kentucky
Mrs. Walter A. Porter—Virginia
Mrs. Edwin R. Guidry—Louisiana
Mrs. E. L. Posey, Jr.—Mississippi
Mrs. Robert D. Moreton—Texas
Mrs. Leo Smith—Georgia

Mrs. Robinson, President, announced that she had no special report, but requested that the four Newsletters which she had sent out during the year constitute her report.

Mrs. Kalford W. Howard, Treasurer, reported a balance on hand, November 10, of $899.76—with the expenses of the Convention and other outstanding bills to be paid before closing the books.

The regular order of business was suspended to welcome Dr. J. P. Culpepper, Jr., President of the Southern Medical Association, and Dr. A. Clayton McCarty, Chairman of the SMA Council. Dr. Culpepper said he considered it a privilege to work with the Auxiliary and complimented Mrs. Robinson on her year's work. He felt it had been good public relations. He said he was proud to be President in the year when the new headquarters office—A Monument to Southern Medicine—was started in Birmingham. He paid tribute to the men who, in 1906, organized the Southern Medical Association in Chattanooga. He assured the Auxiliary that the new building was for the use of the women as well as the men, and that the Executive Committee and the Council was on record as approving the placing of the Jane Todd Crawford Fund in the Building Fund and used to furnish the Auxiliary Room. He thanked the Auxiliary for their fine support.

Dr. McCarty brought greetings from the "Land of Jane Todd Crawford." After several most humorous remarks, he spoke of the pleasure it had been to work with Mrs. Robinson and the Auxiliary. He urged the group to keep up its interest and to continue to "lay bricks." In closing, he said: "We can't get along without you!"

The regular order of business was resumed, and Mrs. Thomas E. Strain reported that the Treasurer's books had been audited and were in good order.

In the absence of Mrs. Charles T. Shepherd, Mrs. John J. O'Connell presented the proposed budget for 1957-58. She moved its adoption and the motion carried.

BUDGET

(1957-1958)

Appropriation from Southern Medical Association		$3,600.00
Convention Expenses (Nov. 1958)	$ 650.00	
Newsletters	200.00	
President (for Auxiliary operations)	200.00	
Stationery	100.00	
President-elect	75.00	
Recording Secretary	10.00	
Historian	5.00	
Treasurer	5.00	
Doctors' Day Awards ($15.00 state, $10.00 each for best large and small counties)	35.00	
Doctors' Day Promotion	40.00	
Past President's Pin	15.00	
Contingency	50.00	
Research and Romance of Medicine	10.00	
Memorial	10.00	
Nominating	15.00	
Membership	10.00	
Councilors (17)—$10.00 each	170.00	
President's Travel (to state conventions and to official meetings)	2,000.00	
		$3,600.00

Mrs. Stanley A. Hill, Mississippi, presented a resolution in appreciation of the many courtesies extended the members of the Auxiliary in Miami Beach. She moved its adoption and the motion carried. Serving on the Courtesy Resolution Committee with Mrs. Hill were Mrs. Elias Margo, Oklahoma, and Mrs. Edwin L. Guidry, Louisiana.

The President requested the reading of the resolutions which had been recommended by the Preconvention Board: 1. A recommendation from the Doctors' Day Committee that exhibits should be in a separate classification and not considered in judging as part of the best Doctors' Day observance. Mrs. W. G. Thuss moved its adoption which carried. 2. A resolution that the money remaining in the Jane Todd Crawford Fund be used in the Woman's Auxiliary Room in the new headquarters building of the Southern Medical Association in Birmingham, including a large bronze plaque for the door of said room and a painting of Jane Todd Crawford and the remainder of the Fund in furnishings for this room. Mrs. Roy A. Douglass moved the adoption of this resolution which was seconded by Mrs. K. W. Howard and carried. 3. A resolution that all revisions be recommended for study to the incoming Executive Board, and that we recommend the preparation of a revised Constitution and By-Laws to be presented at the 1958 Convention. Mrs. Perry Melvin moved the adoption of this resolution which was seconded by Mrs. W. G. Elliott and carried.

The President thanked Mrs. J. Ullman Reaves for serving as Parliamentarian for Mrs. Arthur A. Herold who was temporarily absent.

Mrs. Guidry read several telegrams of greetings and good wishes from friends and absent members.

The President requested the Secretary to read Constitution and By-Law provisions pertaining to nominations and elections. She then asked for nominations for members of the Nominating Committee for 1958. Those nominated from the Board were: Mrs. Oscar W. Robinson, Mrs. John J. O'Connell, and Mrs. Thomas E. Strain. Mrs. Guidry moved the nominations closed which was seconded by Mrs. William Ray Moore and carried. Nominations from the membership were Mrs. Gerald Le Van and Mrs. W. G. Elliott. Mrs. Stanley Hill moved that the nominations be closed which was seconded and carried. Mrs. W. W. Hubbard moved that the above nominees be elected which was seconded and carried.

A slate of officers for 1957-58 was presented by Mrs. O'Connell who was Acting Chairman of the Nominating Committee in the absence of Mrs. V. Eugene Holcombe, the Committee being composed of Mrs. Holcombe, Mrs. O'Connell, Mrs. Shelley Davis, Georgia, and Mrs. Roy Douglass, Tennessee. The nominees for the various offices were:

President—Mrs. Walker L. Curtis, College Park, Georgia

President-Elect—Mrs. George Owen, Jackson, Mississippi

Vice-Presidents—Mrs. Kalford W. Howard, Portsmouth, Virginia; Mrs. John M. Brewer, Kershaw, South Carolina; Mrs. J. R. Horn, Jr., Bessemer, Alabama.

Treasurer—Mrs. Ross P. Daniel, Beckley, West Virginia

Recording Secretary—Mrs. William A. Garrott, Cleveland, Tennessee

Historian—Mrs. J. Ullman Reaves, Mobile, Alabama

Mrs. O'Connell moved the election of the above slate. The motion was severally seconded and carried.

The incoming President, Mrs. Curtis, appointed the following officers:

Corresponding Secretary—Mrs. Leo Smith, Waycross, Georgia

Parliamentarian—Mrs. Shelley Davis, Atlanta, Georgia

The installation of officers was conducted by Mrs. James N. Brawner, Sr., Atlanta, a Past-President of the Auxiliary. Each officer was instructed in her duties in a most impressive manner.

The immediate Past-President, Mrs. O'Connell, presented the Past-President's Pin to the retiring President, Mrs. Robinson, and she, in turn, presented the President's Pin to Mrs. Curtis. Mrs. Curtis accepted the symbols of service and pledged thought and devotion to the advancements which typify the spirit of the Auxiliary and pledged to uphold the prestige of the Auxiliary.

Mrs. Robinson was presented a gift from the Auxiliary to the Texas Medical Association and Mrs. Curtis received a gift from the Georgia Auxiliary.

The Convention adjourned its Annual Meeting at 11:45 a.m.

MRS. OSCAR W. ROBINSON, *President*
MRS. WILLIAM A. GARROTT, *Recording Secretary*

Mrs. Ross P. Daniel, Treasurer, stated that she would send vouchers as soon as possible.

The President announced the Reading Committee for Postconvention Board minutes as follow: Mrs. John M. Brewer, Mrs. Walter A. Porter, and Mrs. William J. Rein. Mrs. J. Ullman Reaves, Historian, requested that materials be sent to her promptly.

Mrs. W. G. Thuss, Sr., Chairman of the Jane Todd Crawford Memorial Committee, pledged her sincere efforts toward the project, and Mrs. J. N. Brawner made the following motion: "Whereas the Jane Todd Crawford Fund has been discontinued in the Southern Medical Auxiliary, I move that the local auxiliaries be requested to make donations to the (SMA) Building Fund." The motion failed.

The Secretary was asked to read from the Handbook, Section 2, which gives the duties of the Councilors.

The President urged that Doctors' Day be emphasized as a public relations project, and to stress the contributions which doctors have made.

Under new business, according to the Constitution, Article V, Section 2, two members were elected to the Executive Board: Mrs. George Owen, Mississippi, and Mrs. Kalford W. Howard, Virginia, Vice-President.

The following Committee Chairmen were announced by Mrs. Curtis:

Special Committee—Auditing—Mrs. Edgar E. Quayle, Washington, D. C.

Standing Committees—

Budget—Mrs. C. T. Shepherd, Missouri
Program—Mrs. C. Grenes Cole, Louisiana
Custodian of Records—Mrs. W. W. Potter, Tennessee
Jane Todd Crawford Memorial—Mrs. W. G. Thuss, Sr., Alabama
Revisions—Mrs. Milford O. Rouse, Texas
Doctors' Day—Mrs. Paul Gray, Arkansas
Membership—Mrs. Kalford W. Howard, Virginia
Memorial—Mrs. Alfred F. Burnside, South Carolina
Publicity—Mrs. Perry D. Melvin, Florida
Research and
Romance of Medicine—Mrs. George H. Garrison, Oklahoma
Resolutions—Mrs. Karl Winter, Kentucky

Councilors (two years)

Alabama—Mrs. William P. Noble
Arkansas—Mrs. L. Gardner
District of Columbia—Mrs. W. J. G. Davis
Florida—Mrs. Eugene F. McCall
Georgia—Mrs. Stephen W. Brown
Louisiana—Mrs. William J. Rein
Maryland—Mrs. Ross Pierpont
North Carolina—Mrs. E. M. Robertson

Councilors (one year)

Kentucky—Mrs. William Ray Moore
Mississippi—Mrs. E. L. Posey, Jr.
Missouri—Mrs. Martyn Schattyn
Oklahoma—Mrs. Elias Margo
South Carolina—Mrs. E. Gordon Able
Tennessee—Mrs. Roy A. Douglass
Texas—Mrs. Robert D. Moreton
Virginia—Mrs. Walter A. Porter
West Virginia—Mrs. W. Dewey Bourne

Mrs. Oscar W. Robinson was named Chairman of the Nominating Committee for 1958.

Mrs. Boni J. DeLaureal, President of the Woman's Auxiliary to the Louisiana State Medical Society, and Mrs. William J. Rein, Councilor from Louisiana, extended a gracious invitation to the meeting in New Orleans, November 3-6, 1958.

The meeting was adjourned at 11:45 a.m., November 13, 1957.

Mrs. Walker L. Curtis, *President*
Mrs. William A. Garrott, *Recording Secretary*

DOCTORS' DAY LUNCHEON

Immediately following the adjournment of the General Session, the Doctors' Day Luncheon was held in the Blue Room of the Delano, November 12, 1957.

Mrs. W. G. Thuss, Sr., Birmingham, Doctors' Day Chairman, presided and presented the Reverend John G. Shirley, Rector, St. Philip's Episcopal Church, Coral Gables, who gave the invocation.

Following the Luncheon, Mrs. Thuss greeted the guests and presented a large number of official guests who were at the Speaker's table.

The entertainment was a playlet written by Lydia Mikell, member of the Woman's Auxiliary to the Dade County Medical Association which was narrated by Mrs. William P. Smith, and produced by Mrs. Greenfield. The title of the playlet was "A Day in the Doctor's Office." The cast consisted of members of the Dade County Auxiliary.

Mrs. Thuss presented Mrs. John J. O'Connell, Chairman of the Doctors' Day Judging Committee who announced the 1957 winners as follow:

1. Best Statewide Observance—First Prize.....Florida
   Honorable Mention, Virginia
2. Best Observance by County with Over 50 Members—
   First Prize .....Tulsa County, Oklahoma
   Honorable Mention, Forsythe-Stokes County, North Carolina
3. Best Observance by County with Less Than 50 Members—
   First Prize ..... Sumter County, Georgia
   Honorable Mention, Seminole County, Florida
4. Feldner Cup (Awarded to a state for best county observance).....Florida for Dade County Observance

Mrs. Thuss thanked the group for making the Luncheon a success and especially Mrs. Henry H. Bryant III, Chairman on Arrangements. Mrs. William P. Smith, Convention Chairman, introduced Mrs. Nicholas A. Tierney, Decorations Chairman, who announced that the orchids which were used in decorating the tables were gifts to the guests.

Mrs. Walker L. Curtis, *President*
Mrs. William A. Garrott, *Recording Secretary*

POSTCONVENTION BOARD MEETING

The Postconvention meeting of the Executive Board was held November 13, 1957, in the Hospitality Room of the Delano.

The business session was preceded by a breakfast. Mrs. Walker L. Curtis, President, introduced Mrs. R. F. Stover, Miami, who gave the invocation.

Following the breakfast, Mrs. Curtis introduced the special guests. Among these was Dr. W. Kelly West, Oklahoma, President-Elect of the Southern Medical Association. Dr. West pledged cooperation with the Auxiliary, offering his help to the officers at any time. Others presented were Mrs. Kelly West, a Past-President of the Auxiliary, Mrs. O. W. Robinson, immediate Past-President, Mr. C. P. Loranz, fondly known as "Mr. Southern Medical," and Mr. V. O. Foster, Executive Secretary. Mr. Foster expressed appreciation to the President and the Auxiliary for the generous contribution to the SMA's Building Fund, and described the Auxiliary Room which will be in the SMA building.

The Board members were requested to introduce themselves. Officers present, nine; Committee Chairmen, eight; Councilors, twelve; and Past-Presidents, seven.

The minutes of the Postconvention Board Meeting for 1956 had been approved and published in the *Southern Medical Journal*. Mrs. Roy Douglass, Tennessee, moved that the reading of the minutes be omitted. The motion was seconded and carried.

SOUTHERN MEDICAL NEWS

ALABAMA

Dr. Albert E. Casey has been succeeded by Dr. Robert M. Cothran as President of the Medical Staff of the Birmingham Baptist Hospitals. The new Vice-President of the Staff is Dr. James F. Crenshaw, and Dr. John W. Rose is Secretary. Dr. Byrn Williamson and Dr. J. W. Underwood have been elected to five year terms on the Executive Committee, and Dr. George S. Graham, Dr. B. H. Johnson and Dr. E. B. Pitts have been elected to one year terms. Dr. Walter Haynes, Dr. A. E. Casey, Dr. D. C. Donald, and Dr. J. D. Heacock are serving unexpired terms.

Dr. Prince P. Barker has been appointed Manager of the VA Hospital in Tuskegee.

Dr. Edwin Ronwin has joined the Biochemistry Department of the University of Alabama Medical Center.

Dr. Paul P. Salter, Jr., Birmingham, was elected President of the Birmingham Academy of Medicine at the annual meeting in January.

Dr. Arthur I. Chenoweth, Birmingham, was elected President-Elect of the Alabama Chapter, American College of Surgeons at the annual meeting at Point Clear in February.

ARKANSAS

Dr. R. B. Robins has recently been appointed Clinical Professor of Medicine at the University of Arkansas.

Dr. William A. Snodgrass, Jr., Little Rock, is the newly elected Vice-President of the Arkansas State Medical Board.

Dr. Paul Mahoney has been named President-Elect of the American Otorhinologic Society for Plastic Surgery.

Dr. James L. Pickens has been elected to active fellowship in the American Academy of Ophthalmology and Otolaryngology.

Dr. Fred Gordy, Conway, has been accepted as a senior member of the American Society of Anesthesiology.

Dr. Edwin S. Chappell has been elected Secretary-Treasurer of the Southern Psychiatric Association.

Dr. Paul K. Kuroda, Associate Professor of Chemistry at the University of Arkansas, has been named to the post of Associate Chemist at Argonne National Laboratory, where he will conduct research on problems of low-level radioactivity.

Dr. Theodore C. Panos, formerly of Galveston, Texas, is now Chairman of the Department of Pediatrics at the University of Arkansas Medical Center in Little Rock.

Dr. Samuel B. Thompson, Little Rock, has been installed as Treasurer of the American Academy for Cerebral Palsy.

Dr. J. Max Roy, Forest City, was installed President of the Mid-South Post Graduate Medical Assembly at the annual meeting in Memphis in February.

DISTRICT OF COLUMBIA

Dr. Maurice Hilleman has accepted appointment as a Director of the Merck Institute for Therapeutic Research.

Dr. Linus A. Zink succeeds Dr. Frank B. Brewer as Assistant Chief Medical Director for Operations in Veterans Administration.

FLORIDA

Dr. Thomas Gowin has been accepted into fellowship in the American College of Surgeons.

Dr. Chester Cassel has been made a Fellow of the American College of Physicians.

Dr. Joseph J. Zavertnik has been appointed to the Florida Cancer Council.

Dr. Milton S. Saslaw has been appointed Governor in the American College of Cardiology for the State of Florida.

Dr. Peter F. Ragan III has been appointed Chairman of the Department of Psychiatry in the University of Florida's J. Hillis Miller Health Center.

Dr. Louis M. Orr, Orlando, attended the Eleventh General Assembly of the World Medical Association held in Istanbul, Turkey, as a member of the Board of Directors.

Drs. Ruth S. and Eugene L. Jewett, Orlando, attended the annual meeting of the Society of Orthopedic Surgery and Traumatology held in Colombia, South America.

Dr. Wilson T. Sowder, Jacksonville, has been elected a Director of the State and Territorial Health Officers Association.

Dr. William M. C. Wilhoit of Pensacola has been elected President of the Florida Mental Health Association.

Dr. Mason Trupp, Tampa, has been awarded a citation for his distinguished work in medicine by the Washington College Alumni Association.

Dr. Reuben J. Plant, Jr., St. Augustine, has been re-elected President of the St. Johns County Welfare Federation.

Dr. Albert V. Hardy of Jacksonville is to fill the recently created position of Assistant State Health Officer.

Dr. Howard V. Weems has been honored for his 35 years of service to the community by the Sebring Rotary Club.

Dr. Henry G. Morton of Sarasota has been installed as President of the Florida Pediatric Society. Dr. Harry M. Edwards of Ocala will serve as Secretary and Dr. Fred I. Dorman of Lakeland as Treasurer.

Dr. Aubrey Y. Covington, Starke, has been elected First Vice-President of the Florida Health Officers Association.

Dr. Arthur C. Allen is a new Professor of Pathology at the University of Miami Medical School.

Dr. Benon H. J. Przybielski has become Assistant Professor of Chemistry at Florida State University.

The Annual Meeting of the Gulf Coast Clinical Society will be held in Pensacola, on Thursday and Friday, October 23-24, 1958. For further information write Dr. J. J. Baehr, Jr., 1117 North Palafox Street, Pensacola, Florida.

The 6th Congress of the Pan American Women's Alliance is to be held in Miami, April 14-17, with headquarters at the McAllister Hotel.

GEORGIA

Dr. Louis K. Levy has been made a Fellow in the American College of Cardiology.

Dr. Thomas F. Sellers, Sr., has been elected Vice-President of the American Public Health Association.

Dr. L. Minor Blackford has been named to the Executive Committee of the Atlanta Civil War Round Table.

Dr. John M. Howard was selected as one of the leaders for the American College of Surgeons' January meeting.

Dr. J. H. Kite has returned from a trip to Honolulu where he attended the meeting of the Pan-Pacific Surgical Association.

Dr. William L. Dobes has been elected Commodore of the Atlanta Yacht Club for 1958. Dr. Dixon Fowler has been elected Fleet Surgeon.

The title of "Emeritus Professor and Emeritus Chairman of the Department of Medicine of the Medical College of Georgia" has been conferred on Dr. Virgil P. Syndenstricker.

The following faculty appointments have been made at Emory University, Atlanta: Dr. Geoffrey H. Bourne as Chairman of the Department of Anatomy; Dr. David Brandes; Dr. Abdel F. Baradi; and Dr. W. C. Osman-Hill. Dr. Gerhard A. Brecher has been named Professor of Physiology.

Dr. R. A. Day, Jr., has been named Chairman of the Department of Chemistry at Emory University.

KENTUCKY

Dr. Russell L. Hiatt has become Manager of the VA Hospital at Louisville.

New officers of the Louisville Society of Anesthesiologists are as follow: Dr. Everett H. Baker, President; Dr. Clarence H. Likins, Jr., Vice-President; and Dr. Shelton H. Mann, Secretary-Treasurer.

Dr. Alexander J. Steigman of the University of Louisville is spending three months as Visiting Director of Professional Education at the Kauikeolani Children's Hospital in Honolulu, Hawaii.

Dr. Thornton Scott, Lexington, has been installed as President of the Central Society for Clinical Research.

LOUISIANA

Dr. Ernest Carroll Faust has been awarded the Bernhard Nocht Medaille for his contributions to the field of tropical medicine.

Dr. Willard Wirth has been elected Vice-President of the New Orleans Area Council, Boy Scouts of America.

Dr. Edwin L. Zander, New Orleans, has been elected President of the City Park Board.

Dr. James D. Rives has been elected President of the Southern Surgical Association.

Dr. William W. Frye has been named to a committee to judge winners of the Ross Awards for 1958.

Dr. Lawrence Strug has been elected Vice-President of the Southern Thoracic Surgical Association.

Dr. Victor E. Tedesco has been elected Fellow to the American College of Surgeons.

Dr. Elliott Shaw has joined the Tulane University Medical School faculty as Associate Professor of Biochemistry.

Dr. Cecil W. Clark, Cameron, has been honored with two national awards. The American Medical Association honored Dr. Clark by naming him the "General Practitioner of the Year." The Medical Service Society of America presented a plaque and gold key to Dr. Clark for his outstanding accomplishments.

Dr. Ralph M. Hartwell, New Orleans, has been named President-Elect of the American Association of Blood Banks.

MARYLAND

Dr. Stuart M. Sessoms has been appointed Assistant Director of the National Cancer Institute.

Dr. J. L. Rhyne, Baltimore, has become Director of the Bureau of Child Health.

Dr. Henry W. D. Holljes, Baltimore, has been named to fill the newly created post of Senior Medical Supervisor—Medical Care in the City Health Department's Medical Care Section.

Dr. Woodrow Hemphill of Baltimore has been appointed Director of the Bureau of School Health in the City Health Department.

Dr. Morris Chelsky succeeds Dr. Robert E. Farber as District Health Officer for the Western Health District of the City Health Department. Dr. Farber has been named Director of the Bureau of Communicable Diseases.

Dr. Albert E. Goldstein has been appointed Counselor to the Baltimore County Medical Society.

The following have been elected as officers of the Washington County Hospital for 1957-1958: Dr. J. G. Warden, President and Chief of Staff; Dr. O. D. Sprecher, Vice-President; Dr. George Jennings, Secretary; Dr. D. J. Boyer, Assistant Secretary; and Drs. E. F. Poole and R. VL. Campbell, Members of Executive Advisory Committee.

Dr. Giampietro Puppi, Director of the Institute for Physics at the University of Bologna, is serving as a Visiting Professor in the University of Maryland Physics Department this semester. Dr. Cyril Domb, Professor of Theoretical Physics at the University of London, will be at Maryland during the spring and summer in the same capacity.

Dr. Raymond E. Vanderlinde of the University of Maryland has resigned to accept a position in New York.

The Maryland Academy of General Practice has installed the following officers: Dr. Archie Robert Cohen, President; Dr. J. Roy Guyther, President-

Elect; Dr. Katherine V. Kemp, Secretary; and Dr. Harry L. Knipp, Treasurer.

Dr. Harold L. Stewart, Bethesda, received the Ward Burdick Award at the recent banquet of the American Society of Clinical Pathologists and the College of American Pathologists.

MISSISSIPPI

Dr. Ciprijans Garanes, a native Latvian, joins the staff of the University of Mississippi Medical Center as Associate Professor of Pathology.

Dr. Melvin L. Schochet has resigned as Chemist of Mississippi State College to accept a position in Ohio.

Dr. Charles C. Randall has been appointed Chairman of the Microbiology Department at the University of Mississippi Medical Center.

The Mississippi Academy of General Practice has installed the following officers: Dr. John C. Longest, President; Dr. Addison T. Tatum, President-Elect; Dr. Louis F. Rittelmeyer, Vice-President; and Dr. R. J. Moorhead, Secretary-Treasurer.

The annual Cardiovascular Seminar sponsored by the Mississippi Heart Association and the University of Mississippi School of Medicine will be held at the University Medical Center in Jackson, April 2-4, 1958. The five-person guest faculty includes: Dr. Henry T. Bahnson, Johns Hopkins University School of Medicine; Dr. Louis N. Katz, Michael Reese Hospital; Dr. John H. Moyer, The Hahnemann Medical College and Hospital; Dr. Catherine A. Neill, Johns Hopkins University School of Medicine; and Dr. Conger Williams, Harvard University School of Medicine.

MISSOURI

Dr. W. J. Burdette, Frontenac, has resigned as Professor of Clinical Surgery at St. Louis University to accept a position in Utah.

Continued on page 54

BOOKS RECEIVED

The Teaching of Hygiene and Public Health in Europe. By F. Grundy and J. M. Mackintosh. World Health Organization: Monograph Series No. 34. 254 pages. New York: Columbia University Press, 1957. Price $5.00.

The Principles of Therapeutics. By J. Harold Burn, M.A., M.D., F.R.S., Professor of Pharmacology, University of Oxford. 265 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $5.50.

The National Vitamin Foundation, Inc. Report to Board of Governors by the Scientific Director. 81 pages. 1956.

Rheumatoid Arthritis. By Charles L. Short, M.D., Walter Bauer, M.D., and William E. Reynolds, M.D. 457 pages. Cambridge, Mass.: Published for the Commonwealth Fund by Harvard University Press, 1957. Price $7.00.

The Human Brain—From Primitive to Modern. By A. M. Lassek, M.D., Professor of Anatomy, Boston University School of Medicine. 217 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $4.75.

Effect of Radiation on Human Heredity. Report of a Study Group. 168 pages. World Health Organization. New York: Columbia University Press, 1957. Price $4.00.

De Motu Cordis. By William Harvey, M.D., Translated from the original Latin by Kenneth J. Franklin. 111 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $3.50.

General Principles Governing the Use of Food Additives. World Health Organization Technical Report Series No. 129. 22 pages. New York: Columbia University Press, 1957. Price $0.50.

Basic Pharmacology for Nurses. Jessie E. Squire, R.N., M.Ed., Instructor, Hayward-Fairmont School of Vocational Nursing, Hayward, California. 255 pages. St. Louis: The C. V. Mosby Company, 1957. Price $3.50.

Clinical Gastroenterology. By Eddy D. Palmer, M.D., Lieut. Col., Medical Corps, U. S. Army. 616 pages. New York: Paul B. Hoeber, Inc., 1957. Price $18.50.

Methods in Surgical Pathology. By Henry A. Teloh, M.D., Assistant Professor of Pathology, Northwestern University Medical School. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $4.75.

Expert Committee on Insecticides—Seventh Report. World Health Organization. Series No. 125. 31 pages. New York: Columbia University Press, 1957. Price $0.30.

The Dermatologist's Handbook. By Ashton L. Welse, M.D., Assistant Professor of Dermatology and Syphilology, University of Cincinnati College of Medicine. 396 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $15.00.

Plaster of Paris Technique. By Marian English, S.R.N., R.F.N. 122 pages. Baltimore: The Williams and Wilkins Co., 1957. Price $4.00.

The Biologic Basis of Cancer Management. By Freddy Homburger, M.D., Research Professor of Medicine, Tufts University School of Medicine. 348 pages. New York: Paul B. Hoeber, Inc., 1957. Price $10.00.

Extensile Exposure. By Arnold K. Henry, M.B., Dublin; M.Ch. (hon.), Trinity College, Dublin and Cairo, F.R.C.S.I. Second edition. 308 pages. Baltimore: The Williams and Wilkins Company, 1957. Price $10.00.

It Pays to be Healthy. By Robert Collier Page, M.D. 285 pages. New York: Prentice Hall, Inc., 1957. Price $4.95.

Medical Radiation Biology. By Friedrich Ellinger, M.D., Chief Radiation Biologist and Head Pharmacology Division, Naval Medical Research Institute. 699 pages, with a 245 page bibliography. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $20.00.

Technique of Fluid Balance. By Geoffrey H. Tovey, M.D., Director, South West Regional Blood Transfusion Service, Southmead, Bristol, England. 95 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $2.50.

An Introduction to Electrocardiography. By L. Schamroth, M.B., B.Ch. (Rand), M.R.C.P.E., F.R.F.P.S., University of Witwatersrand and General Hospital, Johannesburg, South Africa. 58 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $2.50.

The Infantile Cerebral Palsies. By Eirene Collis, W.R.F. Collis, William Dunham, L. T. Lilliard and David Lawson. 98 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $3.00.

Current Medical Research. A reprint of the articles in the Report of the Medical Research Council for the year 1955-56. London: Her Majesty's Stationery Office, 1957. Price 2s.6d.

BOOK REVIEWS

American Academy of Orthopaedic Surgeons Instructional Course Lectures. Vol. 13

Edited by R. Beverly Raney, M.D., Chapel Hill, N. C. 318 pages. Ann Arbor, Michigan: J. W. Edwards, 1956. Price $12.00.

Beginning in 1943 and missing only 1945, the American Academy of Orthopaedic Surgeons, through its program committee on Instructional Courses, has published an annual volume embodying some of the major papers presented in the Instructional Courses given by leading members in the field of Orthopaedic Surgery during the annual meeting. This, the thirteenth volume, is no less well prepared than its twelve predecessors. Considered in this volume are a wide range of subjects of orthopaedic interest, including a panel discussion of the surgical treatment of degenerative diseases of the hip joint in adults; treatment of congenital dislocation of the hip; treatment of slipping of the upper femoral epiphysis; non-disc sciatica; peripheral nerve injuries; reconstruction of some extensor mechanisms in the extremity; bone diseases in children; osteoporosis; management of open fractures of the extremity; development and growth of bones and joints; anatomy of the knee joint; pathology of tumors of soft tissue; vascular lesions and many other subjects, too numerous to mention.

This book is of inestimable value to the orthopaedic resident and to the orthopaedist practicing his specialty. It will, of course, hold very little interest to physicians outside the orthopaedic field.

Textbook of Medical Physiology

By Arthur C. Guyton, M.D., Professor and Chairman of the Department of Physiology and Biophysics, University of Mississippi School of Medicine. 1,030 pages, 577 figures. Philadelphia: W. B. Saunders Company, 1956. Price $13.50.

Dr. Guyton appears to have done the "near impossible." This one man text on such an extensive subject as Medical Physiology demonstrates a real advantage in uniform perspective and proper balance between the respective parts of physiology. The book, though primarily a pure textbook of physiology, incorporates enough pathology to give the medical student transitional information so that the link with other medical studies is clearer and the whole more easily retained. The book, small (1,030 pages) for the amount of material covered, conserves the student's time in some economy of words. In addition the author has reduced the student's burden by setting in smaller print less important matter which allows some option as to the depths a problem may be followed. Material covered is up to date and with each section an excellent bibliography is included. In addition to the subject matter usually covered by standard physiology texts, this text has an excellent but brief section on nuclear physics, x-rays, and their relationship to the human body.

In attacking this book critically it would seem that the author's fear in being too dogmatic in presentation of principles is certainly without significant foundation. He seems to have organized in excellent fashion the principles garnered from many years of teaching this subject. As a matter of record, the book is so organized that not only would it serve well as a basic text for the student, but also as a ready reference for the practitioner who wishes to review and/or recall the physiology he once knew.

Medical Effects of the Atomic Bomb in Japan

Edited by Ashley W. Oughterson, Clinical Professor of Surgery, Yale University School of Medicine; and Shields Warren, Professor of Pathology, Harvard Medical School. 469 pages. New York: McGraw-Hill Book Company, Inc., 1956. Price $8.00.

This volume, one of eight which have been prepared as a record of the research work done under the Manhattan Project and the Atomic Energy Commission, is an account of the medical effects of the atomic bomb bursts in Japan. This particular volume is the work of the Joint Commission for the Investigation of the Effects of the Atomic Bomb in Japan. Much of what appears in this book has been published previously so there is really nothing new. However, it is a very careful and comprehensive account of perhaps the largest, most sudden and horrible catastrophe ever inflicted by man on his fellow man.

The books begin with a brief account of the events which led to the medical investigation after the bomb bursts in Hiroshima and Nagasaki. The scope of physical damage to the cities, the effects of the blast on medical care and medical care facilities, and an outline of the general effects of the blast on the victims are dealt with in one of the earliest chapters. The number and types of casualties are outlined next, followed by a comprehensive section on clinical observations. A large amount of space is devoted to the hematologic effects on those exposed to irradiation. The final chapter is an extensive one on the pathology of atomic bomb injuries.

The book is exceptionally well-illustrated, concise, and easily understandable even to those uninitiated to the mysteries of atomic energy. There is an extensive bibliography which, along with the contents, should make this volume an excellent reference for teachers, physicians and students.

Group Processes

Transactions of the Second Conference, October, 1955. Edited by Bertram Schaffner, M.D., University Seminar on Communications, Columbia University. 242 pages. New York: Josiah Macy, Jr. Foundation, 1956. Price $3.50.

This report, the second in a series of five, appears to be a verbatim account of a four day conference on the general theme of "Play." The participants were representatives of a variety of disciplines: biology, psychology, psychiatry, ethology and sociology, chiefly.

The conferences were informal with much spontaneous give and take between the participants. Three topics were discussed: "The Message 'This Is Play,'" "Social Structure Among Penguins," and "Neonate-Mother Relationship in Goat and Man." A fourth topic, "Kinesic Analysis of Filmed Behavior of Children" was presented as a description of the methods used in filming and studying group behavior of children. The first three subjects were truly discussed, but too often in a maze of such remotely related material that the thread was lost and not always recovered. In many spots the discussions made stimulating and entertaining reading, a tribute to the excellence of the editing.

In a foreword to this volume the Medical Director of the Josiah Macy, Jr. Foundation, sponsor of the conferences, states "The goal of this conference program is the promotion of communication . . . ". Publication of the discussions is designed to share the conference process with a larger audience. Undoubtedly the conferees were successful in communicating among themselves and with others trained in their disciplines. This reviewer must confess, however, that he was lost time and again as the discussions became obtuse. In this respect the conference goal of "communication" fell short of achievement.

Management of Strokes

By Keith W. Sheldon, M.D. 127 pages. Philadelphia: J. B. Lippincott Company, 1956. Price $3.00.

In the introduction of this handbook the author stresses the need for a proper approach to the diagnosis and management of patients with a cerebral catastrophe. Using instructive and amusing cartoons, the writer points out the necessary (and unnecessary) procedures which might be employed in the differential diagnosis of "strokes." Sections of this volume are devoted to thrombosis, spontaneous and traumatic hemorrhage, vascular anomalies, brain tumors, inflammatory intracranial lesions, drug intoxication and degenerative neurologic disorders as they are implicated in differential diagnosis. Illustrative case reports are included.

The therapeutic use of oxygen, carbon dioxide, tracheotomy and physical therapy is fully discussed. Treatment of the acute phase and subsequent rehabilitation of the patient are fully considered.

This handbook is recommended to medical students, general practitioners and internists.

Notes on Atomic Energy for Medical Officers

By the Royal Naval Medical School, Alverstoke, Hampshire, England. 169 pages. New York: Philosophical Library, 1956. Price $4.75.

Although a small volume there is more information packed into its 169 pages than is apparent at first sight of the book. However, as is stated in the title, the material is really a collection of notes on various topics and readers interested in detailed explanations will have to look elsewhere.

The book is meant to provide basic information for medical officers on the short- and long-term effects of an atomic explosion and the dangers from other kinds of radiological warfare. That only an introduction to these subjects is provided in this book is acknowledged in the preface in which is stated: "Officers who are responsible for planning the defense of ships, military units, and towns may need a wider knowledge of the subject, but this booklet will at least serve as an introduction to the books listed in the bibliography."

Among the topics included in these discussions are: introductory physics; x-rays; atomic structure; natural and artificial radioactivity; ionization; release of atomic energy; some properties of fission products; the explosion of the atomic bomb; the life history of the cell; effects of radiation on cells; effects of radiation on the body; estimation of military hazards; treatment of radiation casualties; monitoring instruments; protection against radiation.

Appendixes include a periodic chart of the elements; a table of constants; a bibliography; a glossary; and a discussion of uses of isotopes, of the hydrogen bomb, and of maximum permissible hazards in industry.

It appears to this reviewer that this book is of value to a rather limited number of people. Those who derive benefit will be the persons who use the book as an outline and go to other sources for detailed information on particular topics. If used in this manner, the cost of the volume is justified.

Lectures on the Scientific Basis of Medicine

Volume IV, 1954-55, 397 pages. New York: John de Graff, Inc., 1956. Price $6.50.

This series of lectures exemplified the importance that must be placed in fundamental experimental observations if the optimum advances in medicine and surgery are to be accomplished. In this volume many important areas of current research interest are reviewed. The authors, who are all British investigators, present a very excellent cross section of current medical research interests in Britain.

The twenty-one subjects selected for presentation include "Nucleoproteins in Cell Structure" by J. N. Davidson, "The Chemistry of the Porphyrias" by C. H. Gray, "The Plasma Proteins" by R. A. Kekwick, "Shock and Burns" by J. P. Bull, "Fat Metabolism" by A. C. Frazer, and "Histochemistry and Its Application to the Basic Sciences" by A. G. Everson Pearse. The lecturers have presented their subjects with unusual clarity and conciseness.

Planning New Institutional Facilities for Long Term Care

By Edna Nicholson, Executive Director, The Institute of Medicine of Chicago. 358 pages. New York: G. P. Putnam's Sons, 1956. Price $4.50.

Medical, social and economic changes in recent years have produced new problems in providing adequate care for the aged, the chronically ill and the disabled. These problems, far from being of a temporary nature, are becoming more acute almost daily, and their solution becomes increasingly more urgent. Although shortages in facilities for medical care are primarily quantitative, in some communities it is the quality of medical care that is chiefly deficient.

In this book the author presents an exceptionally clear picture of the current needs and anticipated future needs. After ten years of practical experience and study, first as Director of the Central Service for the Chronically Ill and currently as Executive Director of the Institute of Medicine of Chicago, Miss Nicholson has become the outstanding authority in this specialized field of medical care. Her book is a comprehensive guide for all who are interested in or responsible for providing long-term medical care for the aged, the infirm and the chronically ill. She discusses the planning of services and facilities; the organization, ownership and operation of new facilities; personnel, the location, design, construction, equipment and cost of the physical plant; the place of the facility in the community's health program; and its affiliation with established hospitals. Miss Nicholson has made a timely contribution toward the solution of one of the most pressing medical problems of the present and the future.

Cybernetics. Circular Causal and Feedback Mechanisms in Biological and Social Systems

Edited by Heinz von Foerster, Department of Electrical Engineering, University of Illinois, Champaign, Ill. Transactions of Tenth Conference, April, 1953, Sponsored by Josiah Macy, Jr. Foundation, New York. Price $2.75.

The ever increasing literature on the existing analogies between the functioning of physical and biological systems is treated in this tenth Macy conference on the subject. This particular publication is highly specialized in its three reports by Grey-Walter on activity of the brain, Bar-Hillel on semantic information and Yuen Ren Chao on language. An appendix is included in which a summary of eleven pages brings together the points of agreement in the previous nine conferences on cybernetics, and a cumulative index for the five published reports of conferences is provided. The reader of the summary is stimulated to the point of wondering whether his "loops" can bring back the necessary memories of the previous conference reports. It also may occur to him that the analogy has a high content of irrelevancy which misleads the one who attempts to apply the known facts between physical and biological systems. The freedom with which participants of the various conferences have disagreed with each other, however reassures him that stereotypy of thought did not prevail. The extensive range of research and stimulus to it that resulted from these excellent meetings of minds becomes apparent and impressive in reading the short summary.

Educating Spastic Children

By F. Eleanor Schonell, Ph.D. 235 pages. New York: Philosophical Library, Publisher, 1956. Price $6.00.

The field of educating the spastic child has been very slow to grow, a fact due, in large part, to our physicians who have either failed or been unable to define the educable potential in these children. The author of this book reveals that out of every 100 cerebral palsied children, approximately 24 are normal or above normal in intellectual power; 27 are dull or slow in learning, and 45 are mentally retarded. The remaining 4 are so badly handicapped that diagnosis is not possible. The Terman Merrill revision of the Stanford Binet intelligence scale is found to be the most suitable for testing cerebral palsied children but, of course, many modifications must be made because of the fact that many of these children have a marked speech deficit or lack manual dexterity or have visual or auditory disturbances which limit their ability to relay information to the examiner. Gradually, however, IQ determinations have become more determinable as the examiners have become more cognizant of the problems of the cerebral palsied child. The author urges that these children be cared for in special schools, adequately equipped for the manifold and diverse problems of teaching the spastic children. For children with higher intellectual capacity and lesser physical disability, it is preferable that these children attend day schools. Certainly, it is necessary for many children to stay at the residential school and for children with lower intellectual levels and with more severe physical disabilities, it is necessary that they attend the residential schools. The attainments of these severely handicapped children in these special schools is nothing short of remarkable and the author is to be congratulated in her presentation of the material.

The book itself is not particularly valuable to the physician, except in that we learn that the cerebral palsied child is an educable member of society. It will find its greatest acceptance among administrators, teachers, social workers, and others working in the broad field of Crippled Children's work who are particularly interested in the field of education of the spastic child which is carried on concomitantly with the medical management of these children. We see that something is at last being done for the exceptional child who is crippled mentally and physically. It is this reviewer's hope that similar type work will be done on an increasing scale for the exceptional child of high intelligence.

The Work of WHO 1955

Annual Report of the Director-General to the World Health Assembly and to the United Nations. Official Records of the World Health Organization No. 67. 241 pages, illustrated. Geneva: World Health Organization. Price $2.00.

This is an excellent account of the work of the World Health Organization during 1955, and it leaves one somewhat in awe of the vast number of programs being carried on all over the world.

Substantial results have been obtained in three categories: (1) communicable disease control, (2) strengthening national health services and (3) raising the standards of education and training for all types of health personnel.

In the field of communicable diseases the main development in 1955 was aimed at the eradication of malaria in the shortest possible time because of the capacity of anophelene mosquitoes to acquire resistance to insecticides. More and more countries are turning to WHO for advice on the ambulatory treatment of tuberculosis as a control measure. A change of emphasis in WHO's approach to this disease took place in 1955 with development of the chemotherapy of

tuberculosis in contrast to BCG mass vaccination which was previously the main effort. Concerning viral diseases, WHO's main interest in 1955 was concentrated on the problems of production and application of a safe and effective vaccine against poliomyelitis. Important advances were made in understanding the epidemiology of trachoma and the importance of insects in transmission.

A very important part of the work of WHO continues to be centered about maternal and child hygiene and nutrition. It is becoming increasingly concerned with problems of aging of populations. The study group convened in 1955 to examine atherosclerosis as a manifestation of the organization's concern with this kind of problem.

WHO's program in mental health continues to emphasize the problems of childhood. The improvement in environmental sanitation, which continues to be one of the most pressing problems in under-developed countries, is being carried out by several governments with the assistance of WHO. An essential part of WHO's work has been and continues to be devoted to education and training. An entirely new field of activity for WHO is on the subject of the peaceful uses of atomic energy. In the field of statistics the outstanding event of the year was the conference convened in February in Paris for the seventh revision of the International Lists of Diseases and Causes of Death.

The details of WHO's programs are covered in a concise, clear manner in this report which can be recommended not only for professional health workers but also for citizens the world over who may be interested in health on an international scope.

A Manual of Fractures and Dislocations

By Barbara Bartlett Stimson, M.D., Director of Department of Bone and Joint Surgery, St. Francis Hospital, Poughkeepsie, N. Y. Third edition, 209 pages, 97 illustrations. Philadelphia: Lea & Febiger, 1956. Price $4.50.

This book has been sufficiently well received through two editions to necessitate the publishing of a third edition. The author states in the preface to the first edition that the handbook is intended primarily for medical students with the hope that general practitioners will find it of value. One feels that the author's goal has been admirably reached.

Part I is devoted to definition, classification and diagnosis of fractures, with a discussion of bone repair, the symptoms and signs of fractures, principles of treatment and details in treatment. Parts II, III and IV consider fractures of the upper extremity, the trunk and the lower extremity, in that order. Practically all common fractures are considered in this manual and conservative treatment is the proper keynote throughout. However, the author appears very ready to offer operative intervention when conservative treatment fails.

Line drawings are used fairly profusely throughout the book and are remarkably clear. Few inaccuracies are noted.

It is to be hoped that more medical students will use this book and that it will find a place in the hands of more interns who are dealing with Emergency Room work.

Dermatology

By Donald M. Pillsbury, M.D., Professor and Director of Department of Dermatology, University of Pennsylvania School of Medicine; Walter B. Shelley, M.D., Associate Professor of Dermatology, University of Pennsylvania School of Medicine; and Albert M. Kligman, M.D., Associate Professor of Dermatology, University of Pennsylvania School of Medicine. 1,282 pages, illustrated. Philadelphia: W. B. Saunders Company, 1956. Price $20.00.

The authors have departed widely from the generally accepted format of dermatology texts. Practically no bibliography is given and for that reason this book would be of less value than others for reference work. Because of this, however, much more useful material is included and much of the usual obsolete reports is eliminated for the practitioner. Approximately one-half of the chapters are concerned with basic principles of anatomy, physiology, diagnosis and therapy. The remainder of the text includes a rather routine grouping of diseases into etiological and topographical categories. The illustrations are excellent and introduces a delightful feature of multiple pictures grouped together, representing different diseases in the same location on the body or of the same morphological type. This will prove quite valuable in differential diagnosis. One especially useful chapter is concerned with drawings of distribution patterns of commonly encountered and confusing dermatoses. Therapeutic suggestions are quite up to date and the authors have taken pains to purge many traditional, though useless, forms of medication, which is in itself a real service.

This book can be highly recommended to the medical student, general practitioner and specialist alike.

The Back and Its Disk Syndromes

By Philip Lewin, M.D., Professor Emeritus and formerly Chairman of Orthopedic Surgery, Northwestern University Medical School; Professor of Orthopedic Surgery, Cook County Graduate School of Medicine, Chicago. 920 pages, 371 figures and 4 color plates. Second edition, thoroughly revised. Philadelphia: Lea and Febiger, 1955. Price $18.50.

This, the second edition of this publication which was previously entitled "Backache and Sciatic Neuritis," has been completely revised and rewritten. The present title, however, is misleading in that the book is much broader in its scope than the title would indicate. In addition to very adequate coverage of the embryology, congenital anomalies, infectious processes, traumatic conditions, mechanical disturbances, disk lesions, and arthritides of the spine, the author discusses various pathologic conditions of the sternum, ribs, scapula, genitourinary tract and nervous system. Each subject is presented in an orderly manner to cover diagnosis, prevention, cause, treatment, and prognosis. The book is particularly recommended for its concise presentation of the differential diagnosis of the conditions causing various kinds of symptoms referable to the spine. Treatment is outlined categorically and in addition to the conservative measures which are primarily stressed;

whenever indicated the surgical procedures which are sometimes necessary are described in detail. The book is concluded with a section on medicolegal aspects of backache and estimation of disability of the back; this is too brief and not lucid enough to be of benefit to a reader who is not already well acquainted with the subject.

In addition to calling upon his vast personal clinical experiences in preparing this manuscript, thirty-five years as abstract editor in orthopedic surgery for the *International Abstracts of Surgery, Gynecology, and Obstetrics* makes the author uncommonly well acquainted with the world literature on the problems of the back and its associated structures. Whereas the book will be of only moderate interest to the orthopedic surgeon who is presumably well acquainted with most of the subject matter presented, it will be most helpful to all other physicians whose practice requires the care of adult patients and of necessity are called upon to examine, and frequently to treat the ever so frequent problems of back pain.

Dictionary of Poisons

By Ibert and Eleanor Mellan. 150 pages. New York: Philosophical Library, 1956. Price $4.75.

This short monograph covers the more common poisons and indicates briefly the means of controlling symptoms of over-dosage prior to calling in the physician. This collection of information is less extensive than other monographs on this same subject, and therefore adds very little to the solution of a very difficult problem which faces the physician in the office and in the hospital emergency room in the course of his daily practice.

The Metabolic Response to Neonatal Surgery

By P. P. Rickham, M.S. (London), F.R.C.S., D.C.H., Consultant Paediatric Surgeon, Liverpool Children's Hospital and Alder Hey Children's Hospital. 82 pages. Cambridge, Mass.: Harvard University Press for the Commonwealth Fund, 1957. Price $5.00.

This monograph is an excellent companion piece to *Metabolic Response to Surgery* by Moore and Ball. The balance studies are charted in a method similar to those of Moore and Ball and comparisons are, therefore, more easily made. While only nine infants are presented in detailed balance studies, this comprises a tremendous amount of work, especially in view of the fact that many new technics had to be developed. Chapter I is devoted to historical notes and a general introduction. Chapter II presents the methods used in the investigations. Chapter III presents the details of the investigations of the nine patients. All patients were less than four weeks of age. Only three of the nine were over three weeks of age. These were included to see if the older infant reacted similarly to the neonate. Chapter IV is a general discussion of the metabolic response of neonates to surgery and includes a summary of the response of adults. Chapter V is devoted to practical applications, many of which are empiric and based on experience with over three hundred neonatal procedures not subjected to balance studies.

Of much interest is the fact that neonates do differ markedly from adults in their response to surgery. He points out the differences in water requirements, absence of marked postoperative weight loss, the ability of neonates to maintain a normal K:N ratio, and the difference in the pituitary-adrenal response.

I believe that this is a valuable monograph for those who have an interest in pediatric surgery, especially neonatal surgery. I think the author should be commended for the patience and care with which he has compiled the data.

The Genesis of the Rat Skeleton—A Laboratory Atlas

By Donald G. Walker and Zolton T. Wirtschafter. 59 pages. Springfield, Illinois: Charles C. Thomas, Publisher, 1957. Price $7.50.

This Laboratory Atlas was written to make available to both students and research laboratories a comprehensive macroscopic demonstration of ossification centers in the rat. This should facilitate investigations in which a quantitative assay of skeletal differentiation and growth is needed. Included is a full description of the procedures for dissection, roentgenography, staining and clearing of the intact skeletons, and photography of the specimens. Labeled sketches and photographs are used to show development of the rat skeleton, starting 17 days after conception. In many instances, actual sized photographs are accompanied by enlargements. There is little descriptive material, but the book is profusely illustrated. The photography is adequate, but not outstanding.

INSTRUCTIONS TO CONTRIBUTORS

Exclusive Publication: Articles offered for publication must be contributed solely to the Southern Medical Journal.

Manuscripts: Manuscripts should be original copy, typewritten, double-spaced, with wide margins. Because of lack of space, it is necessary to limit the number of bibliographic references to twenty. Footnotes and references should conform to the following style:

1. Doe, J. E.: What You Should Know about It, New England J. Med. 243:435, 1950.

Illustrations: Black and white glossy prints, preferably 5 by 7 inches, and drawings in India ink on white paper are required. The author's name, number and indication of top, if doubtful, should be attached. Necessary plates not exceeding six, or one and a half pages, will be furnished by the Journal.

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Business Address: All correspondence related to membership, subscriptions, advertising, and other business should be addressed to the Southern Medical Association, Empire Building, Birmingham 3, Alabama.

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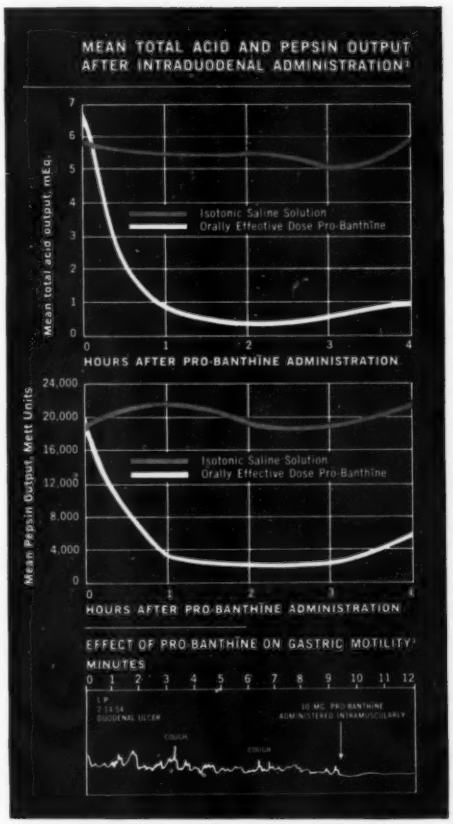
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1. Barowsky, H., in discussion of Barowsky, H.; Schwartz, S. A., and Lister, J.: Experience with Short-Term Intensive Anticholinergic Therapy of Peptic Ulcer, Am. J. Gastroenterol. *27*:156 (Feb.) 1957.
2. Sun, D. C. H., and Shay, H.: Optimal Effective Dose of Anticholinergic Drug in Peptic Ulcer Therapy, Arch. Int. Med. *97*:442 (April) 1956.
3. Lichstein, J.; Morehouse, M. G., and Osmon, K. L.: Pro-Banthīne in the Treatment of Peptic Ulcer, Am. J. M. Sc. *232*:156 (Aug.) 1956.

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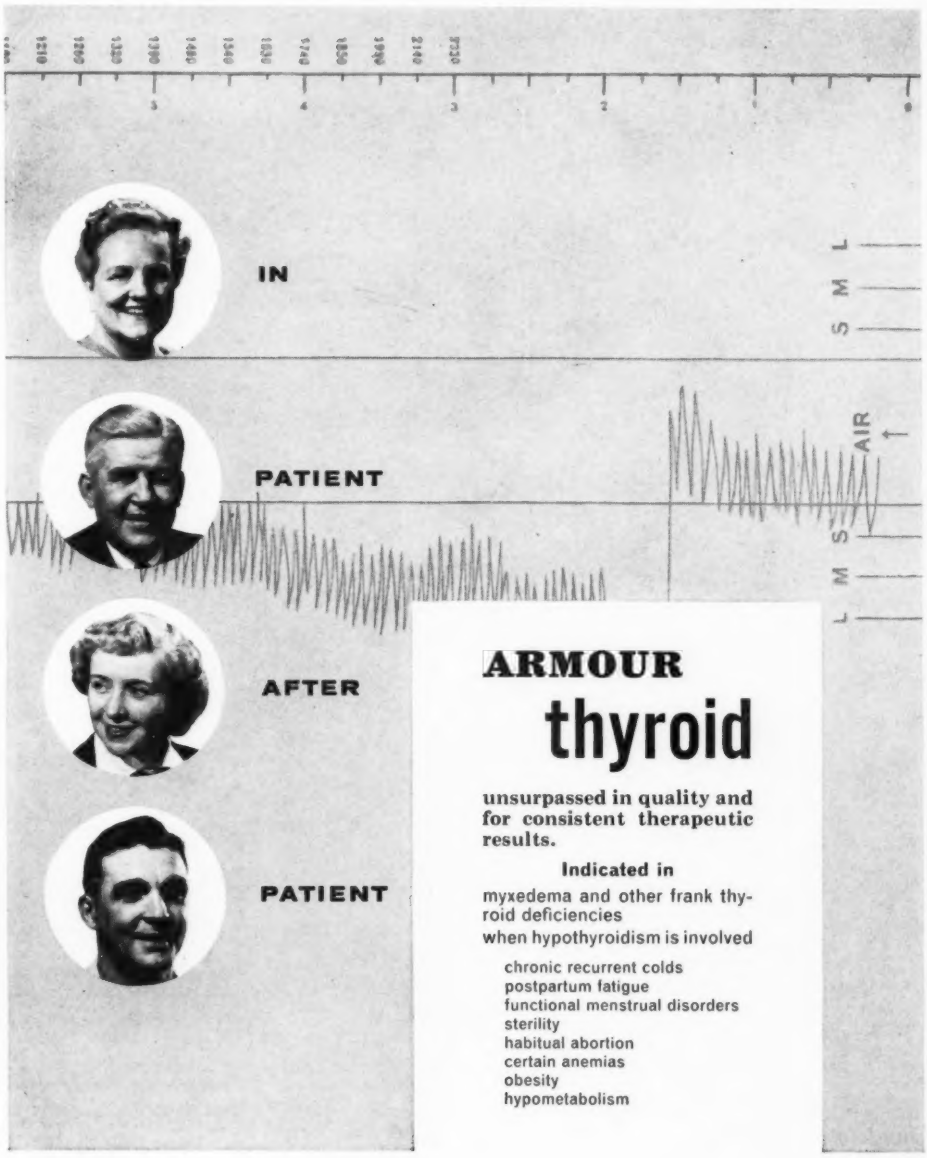

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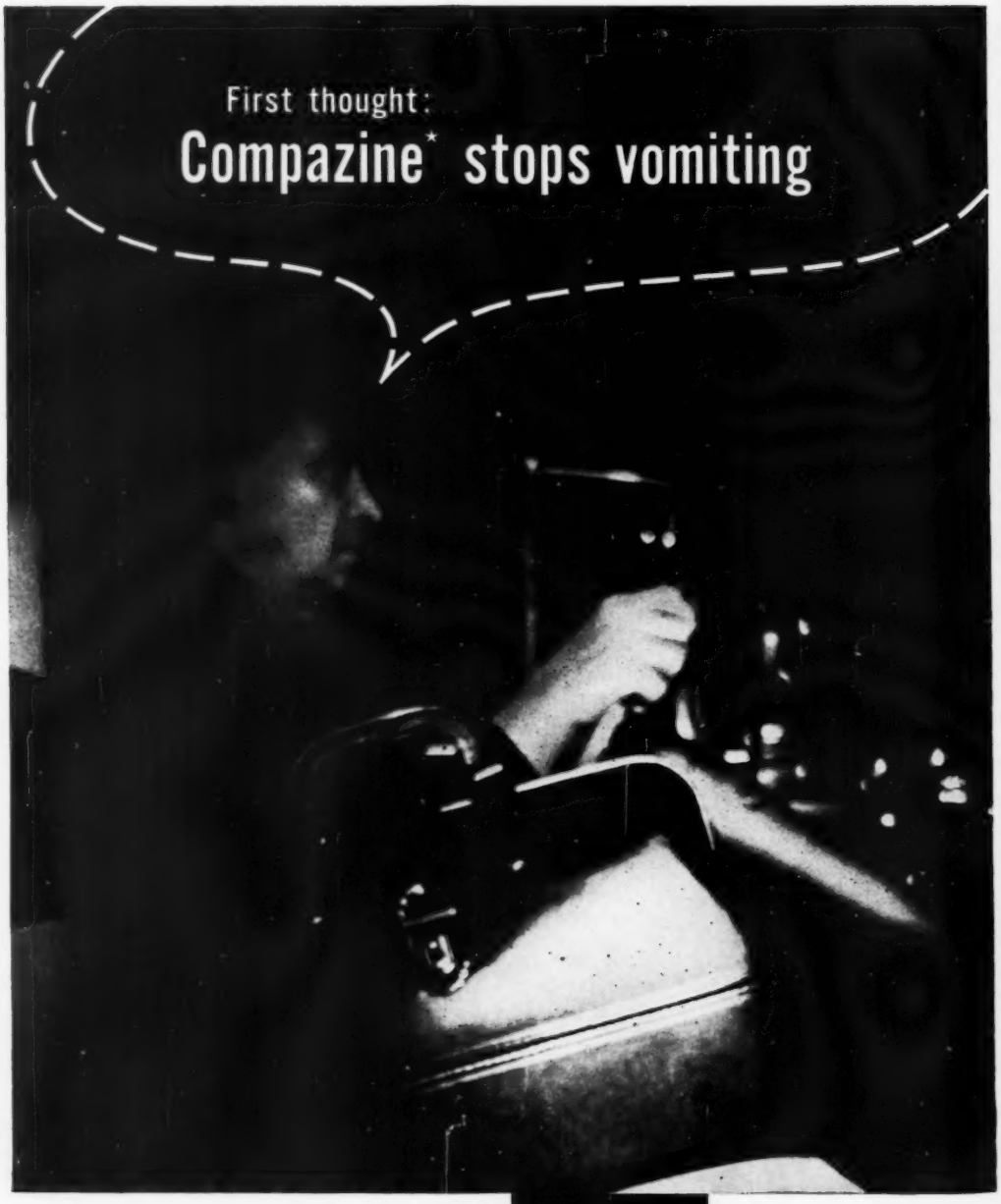

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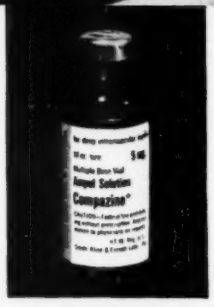

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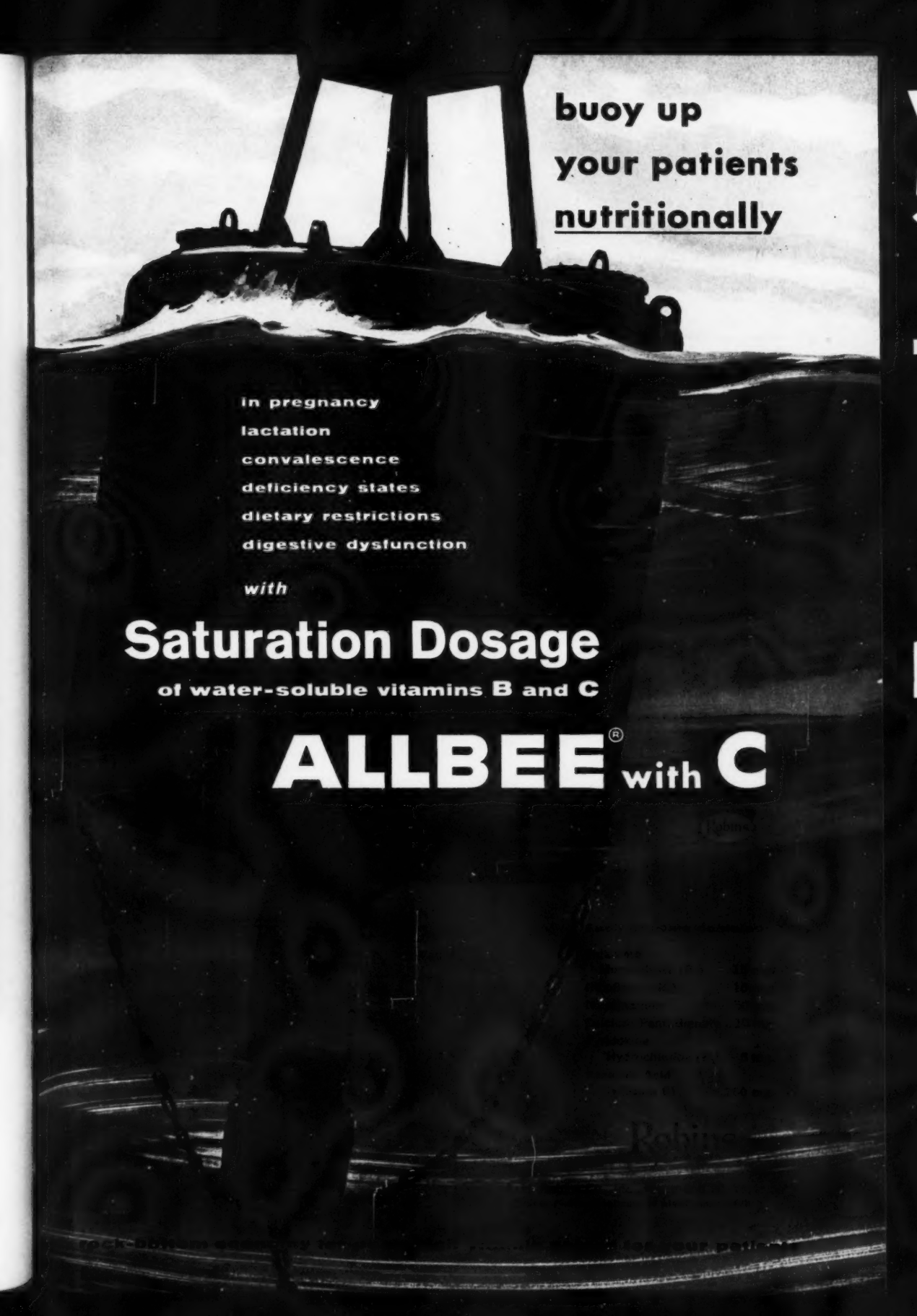
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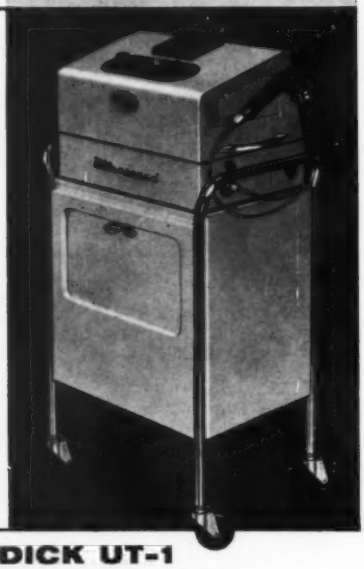

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Continued from page 411

Dr. Ellsworth G. Beers, Seymour, was recently honored for 50 years' membership in the Masonic Lodge.

Dr. Delevan Calkins, Creve Coeur, has been elected President of The Doctors' Medical Foundation.

Dr. Paul M. Beck, St. Joseph, was recently certified a Diplomate of the American Board of Ophthalmology.

Dr. Cyril J. Costello, St. Louis, has been appointed Medical Chief of Staff for a new medical institute which is being built there.

Dr. C. Rollins Hanlon, Director of the Department of Surgery at St. Louis University School of Medicine, was the principal speaker at a session of the Pan-Pacific Surgical Association which recently met in Honolulu.

Dr. Claude J. Hunt has been elected President of the Missouri Division of the American Cancer Society.

Dr. Everett R. Lerwick, St. Louis, was recently elected Chief of Staff of the Missouri Baptist Hospital. Dr. C. H. Kilker was elected Assistant Chief of Staff; Dr. D. E. Kilker, Secretary; and, as members of the Executive Committee, Drs. C. W. Harris, R. D. Brookes, K. V. Larsen and W. M. Lonergan.

Dr. Arthur E. Strauss received the Distinguished Achievement Award of the St. Louis Heart Association.

Dr. B. M. Stuart, Boonville, was recently appointed a member of the Committee on Medical Practice of the American College of Chest Physicians.

Dr. Arthur W. Neilson is the newly elected Head of the St. Louis Medical Society.

Dr. Wendell G. Scott has been appointed Medical Director-at-Large of the American Cancer Society.

Dr. Norton Eversoll has been elected to represent the Missouri Academy of General Practice as a delegate to the American Academy of General Practice.

Dr. Walter C. Gray has been named President of the St. Louis Academy of General Practice. Other officers include: Dr. Charles A. Molden, President-Elect; Dr. Eugene W. Hall, Vice-President; Dr. Eugene V. Henschel, Secretary; and Dr. V. E. Michael, Treasurer.

Dr. Nicholas S. Vitale, St. Louis, has been presented with the Legion of Merit Award of the Italian Republic.

Dr. Richard S. Weiss has returned to his office after a major operation entailing a stay in Barnes Hospital of one month and a recuperative period thereafter.

Dr. James B. Brown, St. Louis, has been installed as President of the Western Surgical Association.

NORTH CAROLINA

Dr. George C. Ham, Professor and Chairman of the Department of Psychiatry, University of North Carolina School of Medicine, has been elected to fellowship in the Academy of Psychoanalysis.

Dr. Hugo Blomquist has retired from the Duke University Botany Department.

Dr. Robert W. Prichard has returned from a two-year tour of duty with the Public Health Service in Bangkok, Thailand.

Continued on page 60

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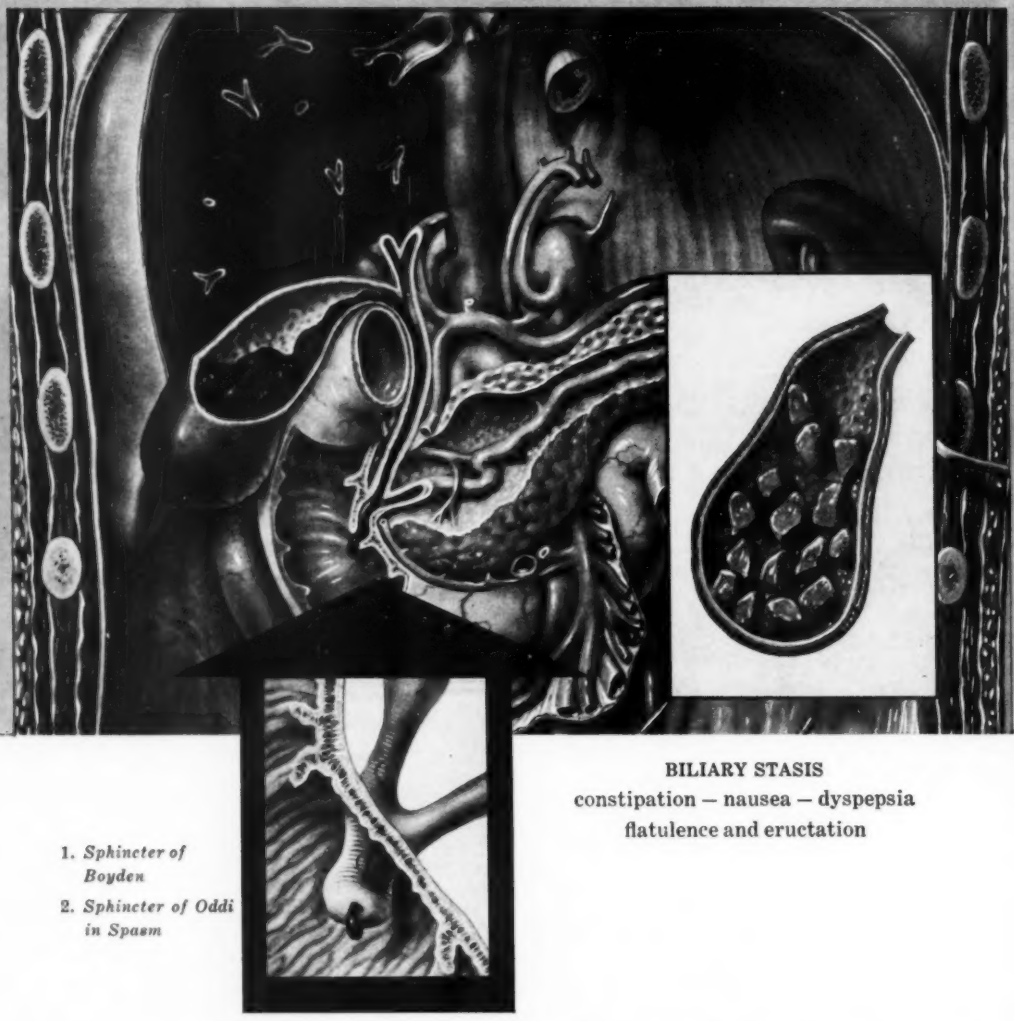

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constipation – nausea – dyspepsia
flatulence and eructation

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Vertigo is a leading complaint among the aged. Help your elderly vertiginous patients with ANTIVERT.

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Continued from page 54

Dr. Norman M. Sulkin, Professor of Anatomy at Bowman Gray School of Medicine of Wake Forest College, has been elected to a three-year term as Council Member, representing the biological sciences of the Gerontology Society.

The Robeson County Medical Society has elected the following officers for 1958: Drs. H. M. Baker, Jr., President; Dr. R. E. Hooks, Vice-President; Dr. D. E. Ward, Jr., Secretary-Treasurer; Drs. C. E. Inman and D. E. Ward, Jr., Delegates; and Drs. John J. Bender and Frank P. Ward, Alternate Delegates.

The Randolph County Medical Society has elected the following officers for 1958: Drs. John Cochran, President; T. R. Cleek, Vice-President; and H. MacM. White, Secretary-Treasurer.

Dr. H. L. Griffin has been made a life member of the North Carolina State Medical Society.

The Seventh Annual Cancer Symposium, sponsored by the Forsyth County Medical Society in cooperation with the Forsyth Cancer Service will be held April 10 at the Hotel Robert E. Lee, Winston-Salem. The following guest speakers have accepted invitations to participate in the Cancer Symposium:

Dr. Ralph Jones, Professor of Medicine, The University of Florida, Miami, Fla.;

Dr. James F. Holland, Hematologist, Roswell Park Memorial Institute, Buffalo, New York;

Dr. James E. Lofstrom, Radiologist, Detroit Memorial Hospital, Detroit, Michigan;

Dr. Charles L. Spurr, Professor of Medicine, Bowman Gray School of Medicine, Winston-Salem, N. C.

The tentative program for the Symposium has been entitled *Recent Advances in Chemotherapy of Leukemias and Lymphomas.* For information write Dr. William H. Boyce, Chairman, Forsyth Cancer Committee, Wake Forest College, The Bowman Gray School of Medicine, Winston-Salem, North Carolina.

Dr. Lenox D. Baker, Orthopedic Surgeon at Duke University, Durham, has been chosen to receive the 1957 Physician's Award of President Eisenhower's Committee on Employment of the Physically Handicapped.

The North Carolina Academy of General Practice has elected new officers. They are as follow: Dr. Charles T. Wilkinson, President; Dr. Charles H. Pugh, President-Elect; Dr. Glenn E. Best, Vice-President; and Dr. John R. Bender, Secretary-Treasurer.

OKLAHOMA

Dr. Charles F. Moore, Durant, was recently presented a Certificate of Life Membership in the Oklahoma State Medical Association.

Dr. Logan A. Spann, Tulsa, has been chosen President-Elect of the Tulsa Academy of General Practice. Other officers are Dr. Thomas W. Taylor, Vice-President; Dr. Harlan Thomas, Secretary-Treasurer; and Drs. Wilmot B. Boone and Earl L. Lusk, Directors.

Members of the newly dedicated Cordell Memorial Hospital are as follow: Dr. L. G. Livingston, Chief of

Continued on page 62

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DR. AMELIA G. WOOD DR. ROBERT K. WILLIAMS

Continued from page 60

the Hospital Medical Staff; Dr. S. Tindall Jones, Assistant Chief of Staff; Drs. Roy W. Anderson, A. H. Bungardt, A. S. Neal, Martin Hale, R. R. Hannas, Jr., A. E. Stowers, Richard F. Shriner, Jr., Wilson Mahone, Lonnie G. Redus, Floyd Simon, Ralph Simon, Ross Deputy, W. C. Tisdal, and Paul Lingenfelter.

The Fourth Annual Surgery, Radiology and Pathology Symposium will be held on March 14 and 15, 1958, at the University of Oklahoma in Oklahoma City. Problems of the pediatric patient related to these fields will be the subject material. The program has been developed by the University of Oklahoma Medical Center and is being co-sponsored by the Oklahoma Chapter of the American College of Surgeons, Oklahoma Association of Radiologists and Oklahoma Association of Pathologists.

Dr. LeRoy D. Long, Oklahoma City, has been installed as Second Vice-President of the Western Surgical Association.

SOUTH CAROLINA

The Columbia Medical Society has elected the following officers: Dr. William S. Hall, President; Dr. John R. Harvin, Vice-President; Dr. R. F. Haines, Secretary; Dr. R. G. Latimer, Treasurer; Dr. Buford S. Chappell, Editor of *The Recorder;* Dr. C. F. Crews, Member of the Board of Censors; Dr. Tucker Weston, Member, Public Relations Committee; Drs. Waitus

Continued on page 84

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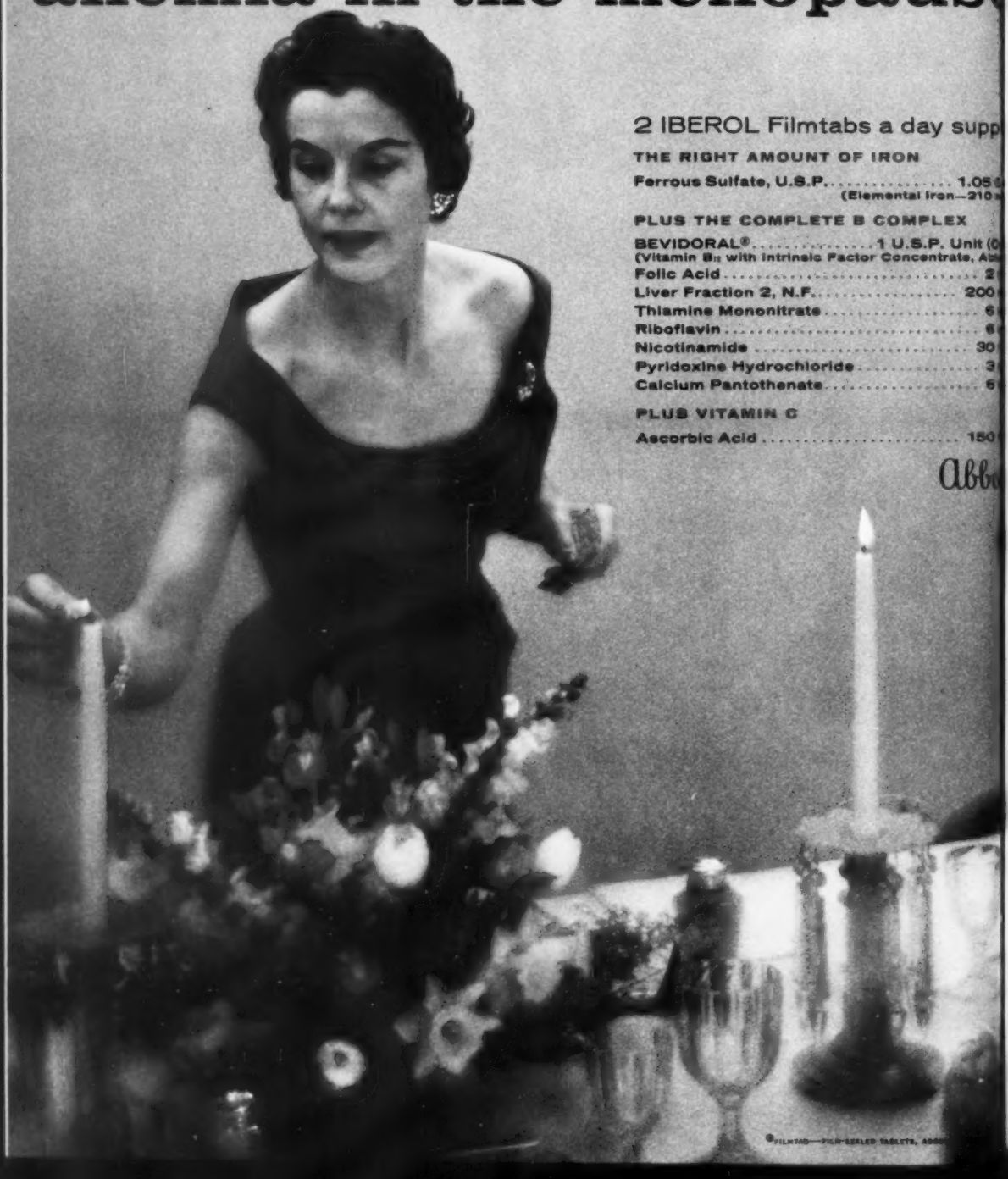

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WHEN YOU TREAT INFECTIONS IN PATIENTS SUCH AS THESE

- debilitated
- elderly
- diabetics
- infants, especially prematures
- those on corticoids
- those who developed moniliasis on previous broad-spectrum therapy
- those on prolonged and/or high antibiotic dosage
- women—especially if pregnant or diabetic

the best broad-spectrum antibiotic to use is

MYSTECLIN-V

Squibb Tetracycline Phosphate Complex (Sumycin) and Nystatin (Mycostatin) — Sumycin plus Mycostatin

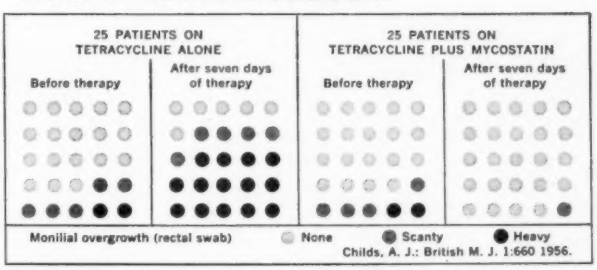
for practical purposes, Mysteclin-V is sodium-free

for "built-in" safety, Mysteclin-V combines:

1. Tetracycline phosphate complex (Sumycin) for superior initial tetracycline blood levels, assuring fast transport of adequate tetracycline to the infection site.

2. Mycostatin—the first safe antifungal antibiotic—for its specific antimonilial activity. Mycostatin protects many patients (see above) who are particularly prone to monilial complications when on broad-spectrum therapy.

MYSTECLIN-V PREVENTS MONILIAL OVERGROWTH



Childs, A. J.: British M. J. 1:660 1956.

Capsules (250 mg./250,000 u.), bottles of 16 and 100. *Half-Strength Capsules* (125 mg./125,000 u.), bottles of 16 and 100. *Suspension* (125 mg./125,000 u.), 2 oz. bottles. *Pediatric Drops* (100 mg./100,000 u.), 10 cc. dropper bottles.

SQUIBB

Squibb Quality—the Priceless Ingredient

'MYSTECLIN,' 'MYCOSTATIN,' AND 'SUMYCIN' ARE SQUIBB TRADEMARKS

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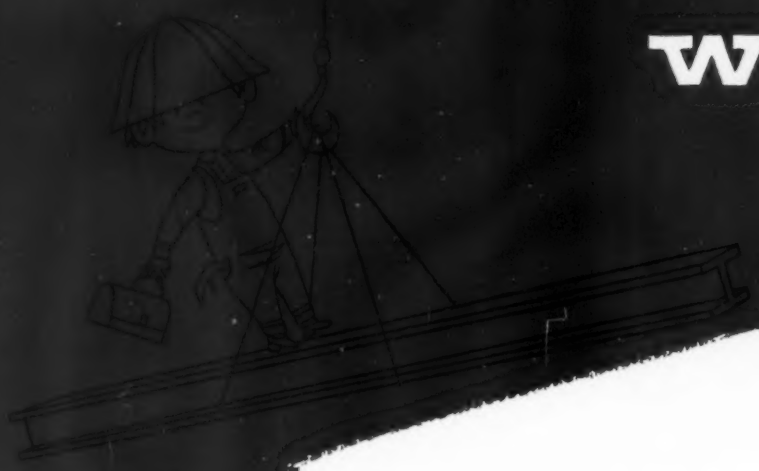


CORRECTS IRON DEFICIENCY AS IT STIMULATES APPETITE

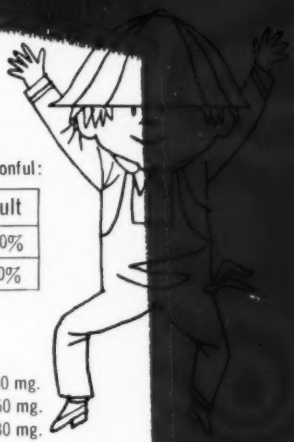
- Offers appetite stimulating Vitamins B_1 B_6 B_{12} and protein-upgrading l-Lysine, fortified with a readily absorbed, well-tolerated form of iron.
- Delicious cherry base designed to appeal to all patients.

PARTICULARILY FOR CHILDREN

Helps young appetites keep pace with the increased nutritional demands of childhood while supplying adequate amounts of essential iron.

REMIN* IRON SYRUP

LYSINE VITAMINS



Provides the following percentages of Minimum Daily Requirements per teaspoonful:

	Child under 6	Child over 6	Adult
B_1	2000%	1333%	1000%
Iron	400%	300%	300%

FORMULA

Each teaspoonful (5 cc.) contains:

l-Lysine HCl	300 mg.
Ferric Pyrophosphate (Soluble)	250 mg.
Iron (as Ferric Pyrophosphate)	30 mg.
Vitamin B_{12} Crystalline	25 mcgm.
Thiamine Mononitrate (B_1)	10 mg.
Pyridoxine HCl (B_6)	5 mg.
Alcohol	0.75%

Average dosage is one teaspoonful daily. Available in bottles of 4 fl. oz.

*Reg. U. S. Pat. Off.

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Lederle

Consistent Gains in Functional Capacity Can Be Achieved with Conservative Therapy

The unemployable arthritic once again may undertake full employment and normal recreation. Patients once confined to the home or wheel chair often find it possible to engage in light work. And even bedridden patients can walk with comfort again. These are the benefits of conservative therapy as demonstrated in long-term studies.[1, 2, 3] In fact, in these four-year comparative studies of salicylate and cortisone, the corticoid showed no superiority.

Superior Conservative Therapy Provided by Buffered Pabirin

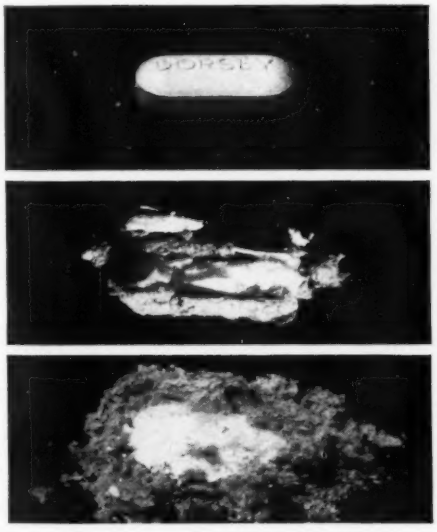
Buffered Pabirin epitomizes modern, conservative therapy without the serious complications of corticoid therapy. Adrenal atrophy, peptic ulcers, moon-face, hypertension or psychotic reactions, a constant risk whenever corticoids are used,[4-7] will not occur with Buffered Pabirin. Month after month, Buffered Pabirin can be administered with a minimum of problems to patient and physician, and without the side effects common to the use of salicylates alone. Buffered Pabirin is sodium and potassium free.

Buffered Pabirin combines new form and formulation for faster pain relief, improved gastric tolerance

Each tablet of Buffered Pabirin consists of an outer layer containing a buffer (aluminum hydroxide), para-aminobenzoic acid and ascorbic acid; an inner core of aspirin. The outer layer quickly releases aluminum hydroxide which affords superior buffering action and protects against gastric irritation. The core of Buffered Pabirin then disintegrates rapidly, permitting fast absorption of acetylsalicylic acid. PABA potentiates the acetylsalicylic acid and thus creates high salicylate blood levels. The ascorbic acid counteracts vitamin C depletion.

The new form and formulation of Buffered Pabirin provides high and sustained salicylate blood levels. It may be administered over long periods of time without the nausea, dyspepsia or other gastrointestinal symptoms so frequently experienced with salicylates alone.

in osteoarthritis, gouty arthritis, rheumatoid arthritis, bursitis, fibrositis, or tendinitis



Photographs show 2-stage Tandem Release disintegration

Buffered Pabirin® *Tablets*

Each tablet contains:

Acetylsalicylic acid (5 gr.) . . 300 mg.
Para-aminobenzoic acid (5 gr.) . . . . . 300 mg.
Ascorbic acid . . . . . 50 mg.
Dried aluminum hydroxide gel . . . . . 100 mg.

Sodium and potassium free.

Dosage: Two or three tablets 3 or 4 times daily.

References: 1. Report of Joint Committee, Medical Research Council & Nuffield Foundation, Treatment of Rheumatoid Arthritis, British Medical Journal (May 29) 1223-1227, 1954. 2. ibid. (April 13) 847-850, 1957. 3. Hart, D.; Bagnall, A. W.; Bunim, J. J., and Polley, F. H.: Ninth International Congress on Rheumatic Diseases, Toronto, Ont. (June 25) 1957. 4. Lewis, L., *et al.*: Ann. Int. Med. *39*-116, 1953. 5. Demartini, F., *et al.*: J.A.M.A. *158*:1505, 1955. 6. Segaloff, A.: Ann. Allergy *12*:565, 1954. 7. Kern, R. A.: Am. J. M. Sc. *233*:430, 1957

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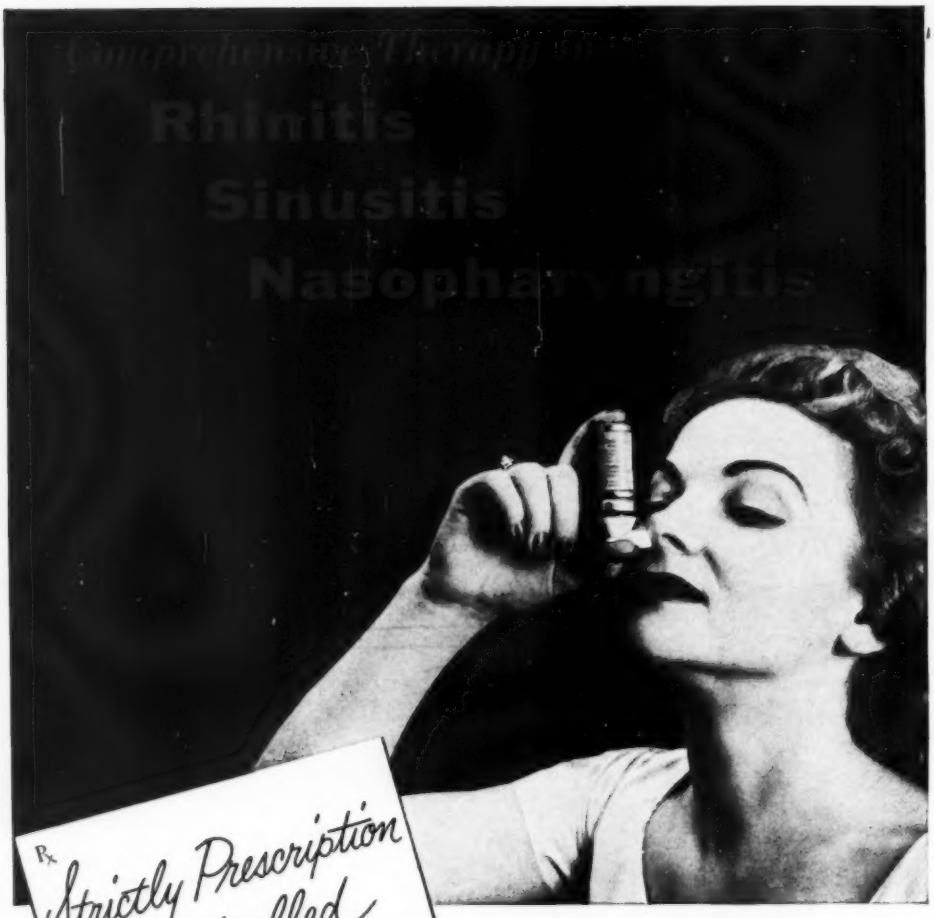

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Immediate, effective 4-pronged relief...vasoconstrictive, decongestive, anti-inflammatory, antibacterial. Accurately measured nebular cloud makes droppers and squeeze bottles obsolete.

Each cc. contains phenylephrine HCl 3.6 mg., phenylpropanolamine HCl 7.0 mg., neomycin sulfate 1.5 mg. (equivalent to 1.0 mg. neomycin base), and hydrocortisone 0.6 mg., suspended in an inert, nontoxic aerosol medium.

Riker LOS ANGELES

MEDIHALER MEANS
automatically measured-dose aerosol medications for closer management supervision over the patient.

1 dose A.M. 1 dose P.M.

are sufficient to combat most urinary and systemic infections of non-viral—non-rickettsial origin. Faster and more prolonged blood levels, plus a new and improved vanilla-mint flavor, make Lipo Gantrisin the ideal pediatric form of Gantrisin. Follow this regimen and note the quick response.

Supplied in bottles of 4 and 16 oz.

Dosage: Teaspoonfuls every 12 hours

Children . .	20 lbs—1	60 lbs—2	(No alkalis or fluids need be given.)
	40 lbs—1½	80 lbs—3	
Adults	4 or 5		

Lipo Gantrisin

ROCHE

Roche Laboratories • Division of Hoffmann-La Roche Inc • Nutley 10 • N. J.

Lipo Gantrisin® Acetyl—brand of acetyl sulfisoxazole in a homogenized mixture Roche—Reg. U.S. Pat. Off.

1 dose A.M.

1 dose P.M.

add up to

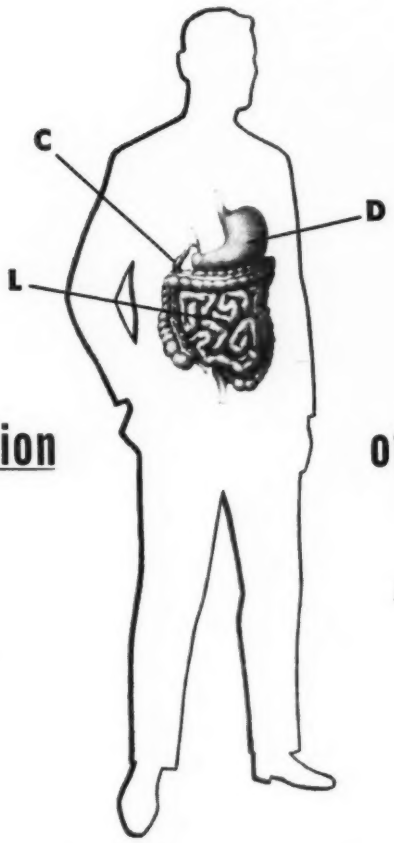
Lipo Gantrisin

ROCHE

- prompt, lasting therapeutic blood levels
- unsurpassed record of effectiveness and safety
- new, improved flavor

relieve the symptoms of constipation

headache
malaise
gas and distention
bad breath
anorexia



treat the causes of constipation

faulty digestion
insufficient flow of bile
poor muscle tone
irregularity

Caroid and Bile Salts tablets help correct:

Faulty digestion – The enzyme, Caroid, improves protein digestion up to 15%.

Insufficient flow of bile – Bile salts increase the flow of bile to maintain normal water balance in the colon for soft, well-formed stools – and to improve fat digestion.

Poor muscle tone – Two gentle laxatives working synergistically provide mild stimulation of the upper and lower bowel.

Irregularity – Caroid and Bile Salts with its (D) digestant (C) choleretic (L) stimulant laxative action encourages return to normal daily bowel function.

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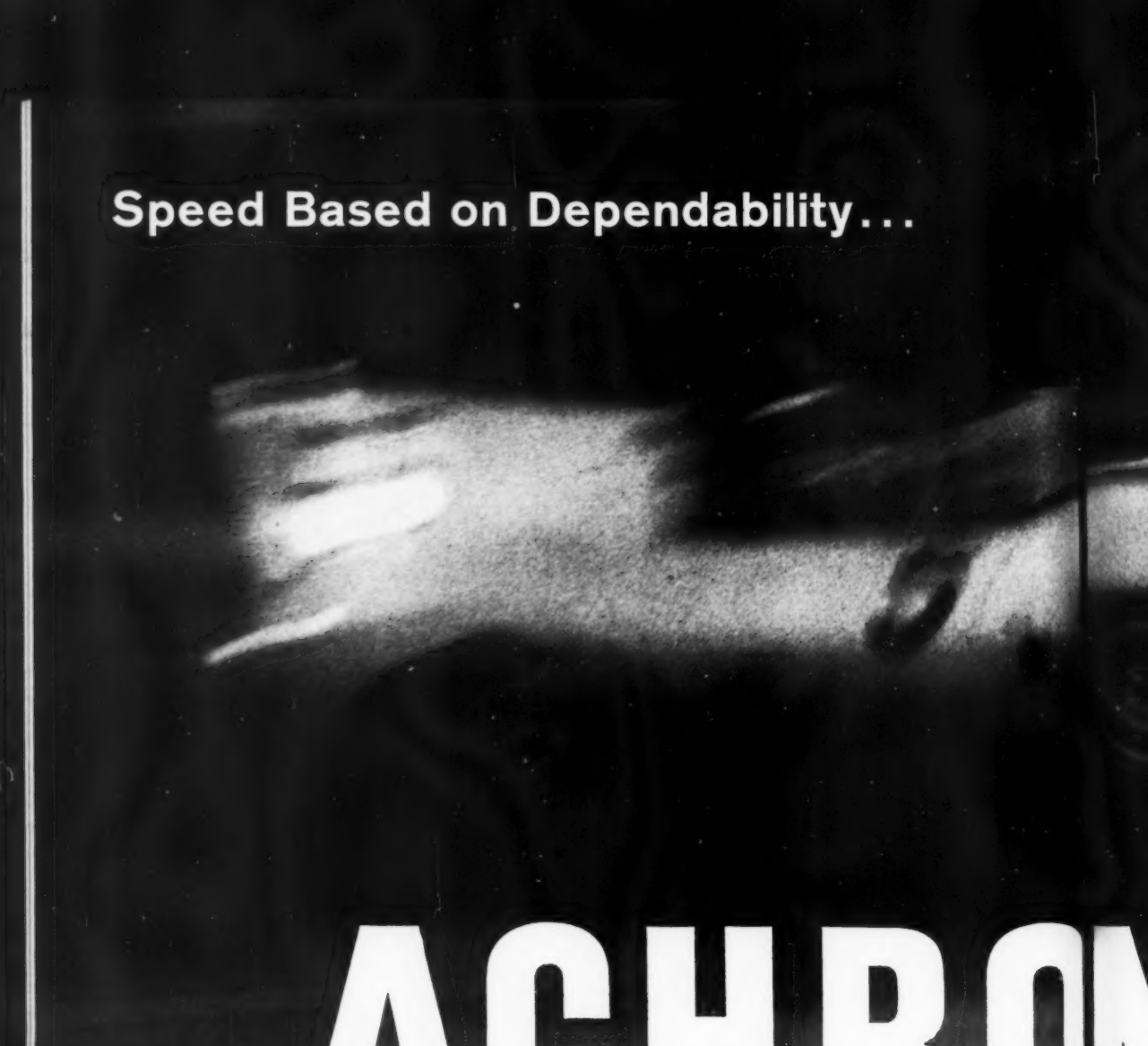
make it a routine practice to have only "regular" patients

Speed Based on Dependability...



ACHRO

ACHROMYCIN Tetracycline serves as the model for the newest advance in broad-spectrum antibiotics. For more than three years it has repeatedly demonstrated exceptional effectiveness in the treatment of more than 50 different infections.

Now speed of absorption has been added to its unsurpassed antibiotic dependability. New ACHROMYCIN V Capsules offer more patients consistently high blood levels...a gain

OMYCIN·V*

Tetracycline HCl Buffered with Citric Acid

in efficiency at no sacrifice to broad, anti-infective spectrum or indications. New ACHROMYCIN V Capsules do not contain Sodium.

REMEMBER THE V WHEN SPECIFYING ACHROMYCIN V

CAPSULES: (blue-yellow) 250 mg. tetracycline HCl (buffered with citric acid, 250 mg.); 100 mg. tetracycline HCl (buffered with citric acid, 100 mg.). **ACHROMYCIN V DOSAGE.** Recommended basic oral dosage is 6-7 mg. per lb. body weight per day. In acute, severe infections often encountered in infants and children, the dose should be 12 mg. per lb. body weight per day. Dosage in the average adult should be 1 Gm. divided into four 250 mg. doses.

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Dosage Forms of Dilaudid hydrochloride:

Ampules: 1 cc., 2 mg. and 3 mg. each.

Hypodermic Tablets: 2, 3 and 4 mg. each.

Oral Tablets: 2.7 mg. each.

Multiple Dose Vial: 10 cc., 2 mg. Dilaudid sulfate per cc.

*Subject to Federal narcotic regulations

Dilaudid®, E. Bilhuber, Inc.

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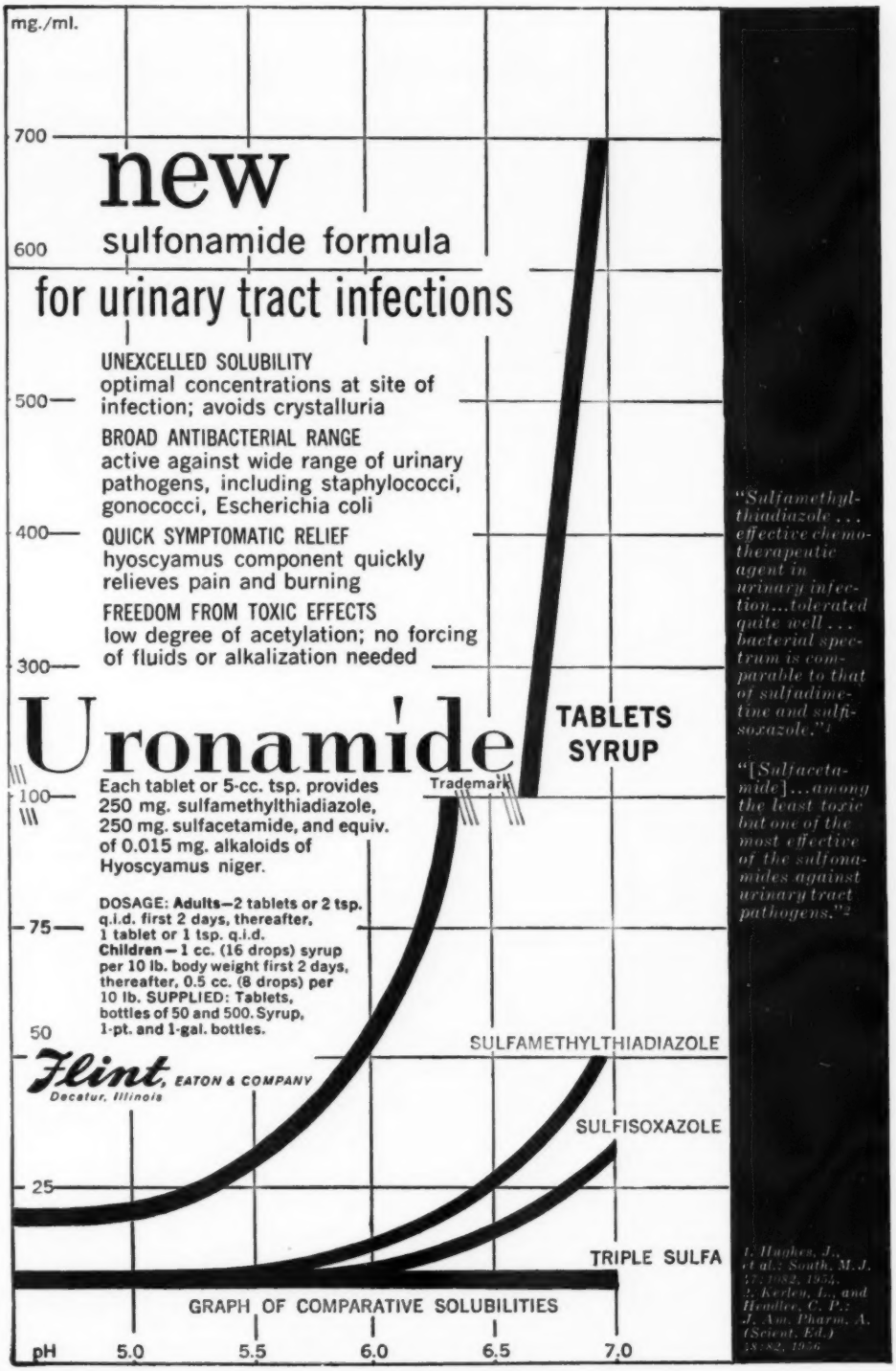

new

sulfonamide formula

for urinary tract infections

UNEXCELLED SOLUBILITY
optimal concentrations at site of infection; avoids crystalluria

BROAD ANTIBACTERIAL RANGE
active against wide range of urinary pathogens, including staphylococci, gonococci, Escherichia coli

QUICK SYMPTOMATIC RELIEF
hyoscyamus component quickly relieves pain and burning

FREEDOM FROM TOXIC EFFECTS
low degree of acetylation; no forcing of fluids or alkalization needed

Uronamide™ TABLETS SYRUP

Each tablet or 5-cc. tsp. provides 250 mg. sulfamethylthiadiazole, 250 mg. sulfacetamide, and equiv. of 0.015 mg. alkaloids of Hyoscyamus niger.

DOSAGE: **Adults**—2 tablets or 2 tsp. q.i.d. first 2 days, thereafter, 1 tablet or 1 tsp. q.i.d. **Children**—1 cc. (16 drops) syrup per 10 lb. body weight first 2 days, thereafter, 0.5 cc. (8 drops) per 10 lb. SUPPLIED: Tablets, bottles of 50 and 500. Syrup, 1-pt. and 1-gal. bottles.

Flint, EATON & COMPANY
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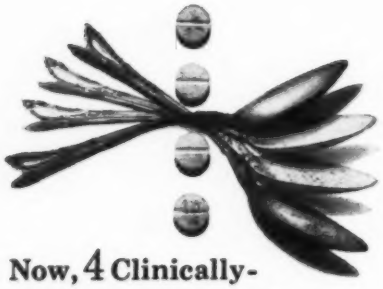
"Sulfamethylthiadiazole ... effective chemotherapeutic agent in urinary infection...tolerated quite well ... bacterial spectrum is comparable to that of sulfadimetine and sulfisoxazole."[1]

"[Sulfacetamide]...among the least toxic but one of the most effective of the sulfonamides against urinary tract pathogens."[2]

1. Hughes, J., et al.: South. M.J. 47:1082, 1954.
2. Kerlen, L., and Headley, C. P.: J. Am. Pharm. A. (Scient. Ed.) 38:82, 1956

Pluralizes Potency 4 Times!



Now, 4 Clinically-Proven Sulfonamides Unite for Safe, Superior Action

Katrasul combines 4 powerful sulfas in one palatable preparation. Provides broad spectrum of activity 4 times as potent as any single sulfa. Toxicity and sensitization reactions approach zero.

Formula includes Sulfadiazine, Sulfamerazine, Sulfamethazine, Sulfacetamide —each notable for antibacterial action.

Use of only fractional dosage of each sulfa results in greater solubility, virtual elimination of crystalluria.

Katrasul combats both gram positive and gram negative bacilli. Effective against both common microorganisms and specific infections.

Delightful coconut-custard flavor invites patient acceptance.

Supplied: gallons, pints, 4 oz. bottles also bottles of 100, 1000 tablets

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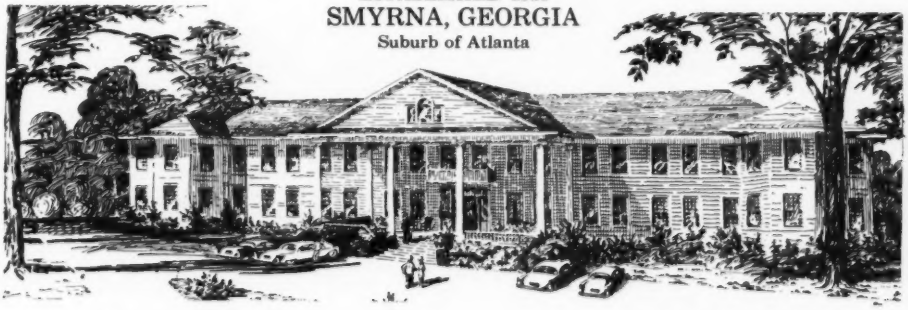

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CHOLOGESTIN contains both ox bile extract and sodium salicylate, plus pancreatin and sodium bicarbonate. Recommended dose as a choleretic or cholagogue, 1 tablespoonful in cold water after meals.

TABLOGESTIN, 3 tablets are equivalent to 1 tablespoonful of Cholagestin.

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HOMAGENETS®

The only homogenized vitamins in solid form

Homagenets are unusually palatable—and good taste is especially important to your patients. Of more interest to the physician is the homogenization process. This presents both oil and water soluble vitamins in microscopic particles. Thus the vitamins in Homagenets are better absorbed and utilized—and stored longer.[1] These are definite advantages to your patient.

1. Lewis, J.M., et al.: J. Pediat. 31:496.

THE ADVANTAGES OF HOMAGENETS

Pleasant, candy-like flavor
Better absorbed, better utilized
Excess vitamin dosage unnecessary
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May be chewed, swallowed or dissolved in the mouth.

Homagenets are available in five formulas: Prenatal, Pediatric, Therapeutic, Geriatric and Aoral (brand of vitamin A).

THE S. E. MASSENGILL COMPANY
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TURN THE PAGE
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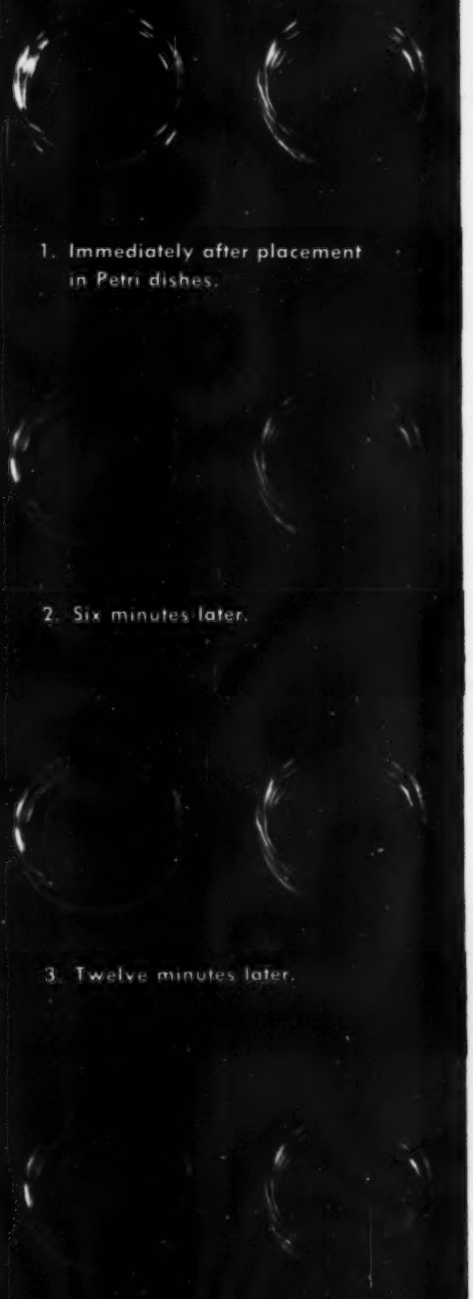
of Homagenets

VISUAL PROOF OF THE RAPID DISPERSION OF HOMAGENETS®



1. Immediately after placement in Petri dishes.

2. Six minutes later.

3. Twelve minutes later.

4. Two hours and 12 minutes later.

These photographs show the dispersion of one of a Homagenet and a soft gelatin capsule in artificial gastric juice at 37° C.

Homagenets are available in five formulas: Prenatal, Pediatric, Therapeutic, Geriatric and Adult dosage of vitamin A.

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"care of the man rather than merely his stomach"[8]

"Milpath" two-level control of gastrointestinal dysfunction

Miltown® + *anticholinergic*

at the central level The tranquilizer Miltown® reduces anxiety and tension.[1, 3, 6, 7] Unlike the barbiturates, it does not impair mental or physical efficiency.[5, 7]

at the peripheral level The anticholinergic tridihexethyl iodide reduces hypermotility and hypersecretion.

Unlike the belladonna alkaloids, it rarely produces dry mouth or blurred vision.[2, 4]

indications: peptic ulcer, spastic and irritable colon, esophageal spasm, G. I. symptoms of anxiety states.

each "Milpath" tablet contains:

Miltown.® (meprobamate WALLACE) ..... 400 mg.
(2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate)

Tridihexethyl iodide ..... 25 mg.
(3-diethylamino-1-cyclohexyl-1-phenyl-1-propanol-ethiodide)

dosage: 1 tablet t.i.d. at mealtime and 2 tablets at bedtime.

available: bottles of 50 scored tablets.

references: 1. Altschul, A. and Billow, B.: The clinical use of meprobamate. (Miltown®). New York J. Med. *57*: 2361, July 15, 1957. 2. Atwater, J. S.: The use of anticholinergic agents in peptic ulcer therapy. J. M. A. Georgia *45*:421, Oct. 1956. 3. Borrus, J. C.: Study of effect of Miltown (2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate) on psychiatric states. J. A. M. A. *167*:1596, April 30, 1955. 4. Cayer, D.: Prolonged anticholinergic therapy of duodenal ulcer. Am. J. Digest. Dis. *1*:301, July 1956. 5. Marquis, D. G., Kelly, E. L., Miller, J. G., Gerard, R. W. and Rapoport, A.: Experimental studies of behavioral effects of meprobamate on normal subjects. Ann. New York Acad. Sc. *67*:701, May 9, 1957. 6. Phillips, R. E.: Use of meprobamate (Miltown®) for the treatment of emotional disorders. Am. Pract. & Digest Treat. *7*:1573, Oct. 1956. 7. Selling, L. S.: A clinical study of Miltown®, a new tranquilizing agent. J. Clin. & Exper. Psychopath. *17*:7, March 1956. 8. Wolf, S. and Wolff, H. G.: Human Gastric Function, Oxford University Press, New York, 1947.

WALLACE LABORATORIES, New Brunswick, N. J.

relaxes both mind & muscle without impairing mental or physical efficiency

well tolerated, relatively nontoxic/no blood dyscrasias, liver toxicity, Parkinson-like syndrome or nasal stuffiness/ well suited for prolonged therapy

Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets. *Usual dosage:* One or two 400 mg. tablets t.i.d.

For anxiety, tension and muscle spasm in everyday practice.

Miltown®

tranquilizer with muscle-relaxant action

2-methyl-2-n-propyl-1,3-propanediol dicarbamate

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DISCOVERED & INTRODUCED BY

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"I don't know what's wrong, Doctor, I'm just off my feed."

You see these "down-in-the-dumps" patients only too often.

The sallow businessman. The listless housewife. The elderly patient who eats next to nothing—and looks it. The lazy, underweight adolescent. Convalescents of all ages.

When you wish to increase appetite, to restore vim, vigor and vitality in the patient who keeps saying, "I just don't feel quite right," prescribe 'Trophite'—the high potency combination of B_{12} and B_1. Each *delicious* teaspoonful, or each convenient tablet, supplies 25 mcg. B_{12} and 10 mg. B_1.

TROPHITE* for appetite

*T.M. Reg. U.S. Pat. Off.

Smith Kline & French Laboratories, Philadelphia

Continued from page 62

Tanner, C. J. Milling, and Frank C. Owens, Delegates; and Drs. W. T. Barron, R. B. Josey, and C. J. Lemmon, Alternate Delegates.

Dr. Victor Branford, Dillon, is President of the Pee Dee Medical Association for 1958.

Dr. Lawrence Hester, Jr., succeeds Dr. Herbert Blake as President of the South Carolina Obstetrical and Gynecological Society.

Dr. James R. Cain has been named Director of the Pathology Laboratory at Spartanburg General Hospital.

Dr. Martin D. Young of the South Carolina State Hospital was on the staff of a training course in malaria eradication technics held in Guatemala and El Salvador.

Dr. William S. Hall is President of the recently organized South Carolina District Branch of the American Psychiatric Association. Other officers are Dr. J. J. Cleckley, Vice-President; Dr. Joe E. Freed, Secretary-Treasurer; and Drs. W. P. Beckman and J. J. Nannarello, Councilors.

Dr. Peter Christopher Gazes, Charleston, has been named a Fellow of the American College of Physicians.

Dr. Lawrence W. Long, Union, has been named winner of the first Hamilton-National Medical Association Award which is given annually to the "general practitioner who is also active in the local and state societies of the National Medical Association."

TENNESSEE

Dr. James W. Culbertson has been appointed Professor of Medicine at the University of Tennessee.

Dr. William H. L. Dornette has assumed duties as Professor and Head of the Department of Anesthesiology at the University of Tennessee.

Dr. Charles W. Sheppard has joined the Department of Physiology at the University of Tennessee Medical School.

Recent additions to the staff of the Medical Division of the Oak Ridge Institute of Nuclear Studies are as follow: Drs. Ryosaku Tanida, Alvin Segel, C. G. Papavassiliou, and Lan-Chang Chiang.

Dr. Rollin A. Daniel, Jr., has been named President-Elect of the Nashville Academy of Medicine. To serve with him is Dr. Thomas S. Weaver as Secretary-Treasurer. Drs. Robert Finks and Joseph Ivie were elected to three year terms on the Board of Directors.

The following doctors have been named Fellows of the American College of Physicians: John S. Powers, Jr., Kingsport; Alvin J. Cummins and Arthur W. Julich, Memphis; and M. J. Mackinnon, Mountain Home. The following were named Associates of the College: Merrill F. Nelson, Chattanooga; Fred D. Ownby and John Thomas, Nashville; and Frank London, Knoxville.

Dr. Raphael N. Paul, Memphis, has been appointed Governor for Tennessee in the American College of Cardiology.

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Dr. Marcus Stewart, Memphis, was recently named President of the Clinical Orthopedic Society.

Dr. John H. Saffold, Knoxville, has been re-elected Chief of Staff at the University of Tennessee Hospital. Dr. John Kesterson, Knoxville, is the new Staff Secretary.

Officers for the Sullivan-Johnson County Medical Society for 1958 are: Dr. W. A. Wiley, Kingsport, President; Dr. J. E. Phillips, Bristol, Vice-President; and Dr. Joseph Fleming, Kingsport, Secretary-Treasurer.

Dr. Amos Christie, Nashville, has been chosen to receive the John Phillips Memorial Award.

Dr. Rufus Morgan has been re-elected Mayor of Pikeville.

Dr. William K. Swann, Knoxville, has been named Chief of Staff of Children's Hospital. Dr. Richard B. Willingham will assist him as Vice-Chief of Staff. Dr. Clifford Walton has been named Secretary.

Dr. Homer Venter, Jr., Chattanooga, has been elected a Fellow of the American Academy of Pediatrics.

The Congress of Neurological Surgeons has elected Dr. Richard L. DeSaussure, Jr., Memphis, as its Secretary-Treasurer.

Dr. Edward M. Kelman has joined the laboratory staff of the Blount Memorial Hospital as an associate.

Dr. Powell M. Trusler succeeds Dr. James W. Richardson as President of the Hamblen County Medical Society. Dr. John H. Kinser is the new Vice-President and Dr. Y. A. Jackson, Secretary-Treasurer.

Dr. Rudolph M. Landry, Chattanooga, has been named to the Advisory Board of the Alumni Association of the Mayo Foundation.

Dr. Robert A. Knight, Memphis, has been chosen President-Elect of the American Academy for Cerebral Palsy.

Dr. C. D. Hawkes, Memphis, has been named President of the Southern Electroencephalography Society.

Dr. Oliver W. Hill, Jr., Knoxville, is the 1958 President of the Knoxville Academy of Medicine. Dr. John D. Moore, Knoxville, has been named President-Elect, Dr. George Mahon, Vice-President, and Dr. Ralph H. Monger, Secretary-Treasurer. Dr. Alvin Weber has been elected to the Judicial Council.

Dr. Duane M. Carr, Memphis, has been named President-Elect of the Baptist Hospital Staff succeeding Dr. C. E. Gillespie.

Dr. Daugh W. Smith, Nashville, has been named President of the Nashville Surgical Society.

The new President of the West Tennessee Cancer Clinic is Dr. E. N. Stevenson.

Dr. Harold Feinstein, Memphis, succeeds Dr. William T. Howard as President of the Medical Staff of St. Joseph's Hospital. Dr. James F. Collins is the new Vice-President and Dr. W. H. Gragg, Jr., Secretary. Dr. George Paullus has been named Chief of the General Practice Section.

Continued on page 86

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Continued from page 85

Dr. Wallace Bigbee has joined the staff of the Gibson County Health Department.

Dr. William G. Pollard has been awarded an honorary Doctor of Divinity degree by Grinnell College.

Officers of the Tennessee Chapter of the American Society of Internal Medicine are: Dr. Laurence A. Grossman, Nashville, President; Dr. Philip B. Bleecker, Memphis, President-Elect; and Dr. Carl C. Gardner, Jr., Columbia, Secretary-Treasurer.

Dr. William G. Stephenson, Chattanooga, was elected President-Elect of the Mid-South Post Graduate Medical Assembly at the annual meeting in Memphis in February.

TEXAS

The following officers have been named for the Private Clinics and Hospitals Association of Texas: Dr. Joe Shepherd, Burnet, President; Dr. Jack Maxfield, Dallas, President-Elect; and Dr. Vance Terrell, Stephenville, Vice-President.

The Texas Academy of Internal Medicine has elected the following officers: Dr. Merton M. Minter, San Antonio, President-Elect; and Dr. George R. Herrmann, Galveston, Vice-President. Dr. A. H. Harris, Dallas, succeeded to the Presidency.

The Society for Pediatric Research has elected Dr. Edward L. Pratt, Dallas, as its President.

Dr. Hamilton F. Ford, Galveston, is the new President-Elect of the Central Neuropsychiatric Association.

Dr. Chester E. Cook, Dallas, has been certified as a Diplomate of the Board of Life Insurance Medicine.

Dr. Leslie Pridgen, San Antonio, has been presented a plaque honoring him for "50 years of unselfish service."

Dr. J. Layton Cochran, San Antonio, has been elected Chief of the Medical Staff of the Southwest Texas Methodist Hospital.

Dr. Russell L. Deter, El Paso, has been installed as Secretary-Treasurer of the Southwestern Medical Association.

Dr. Michael E. DeBakey, Houston, has been elected President of the International Cardiovascular Society for the term 1957-1959.

VIRGINIA

Dr. I. D. Wilson has retired from the Head of the Biology Department of Virginia Polytechnic Institute, and has accepted a position with the International Cooperation Administration as a consultant to universities in India.

The officers of the Virginia Society of Ophthalmology and Otolaryngology for 1958 are: Dr. Emanuel U. Wallerstein, Richmond, President; Dr. Calvin T. Burton, Roanoke, President-Elect; Dr. Thomas M. Winn, Covington, Vice-President; and Dr. Maynard P. Smith, Richmond, Secretary-Treasurer. Serving on the Execu-

Continued on page 92

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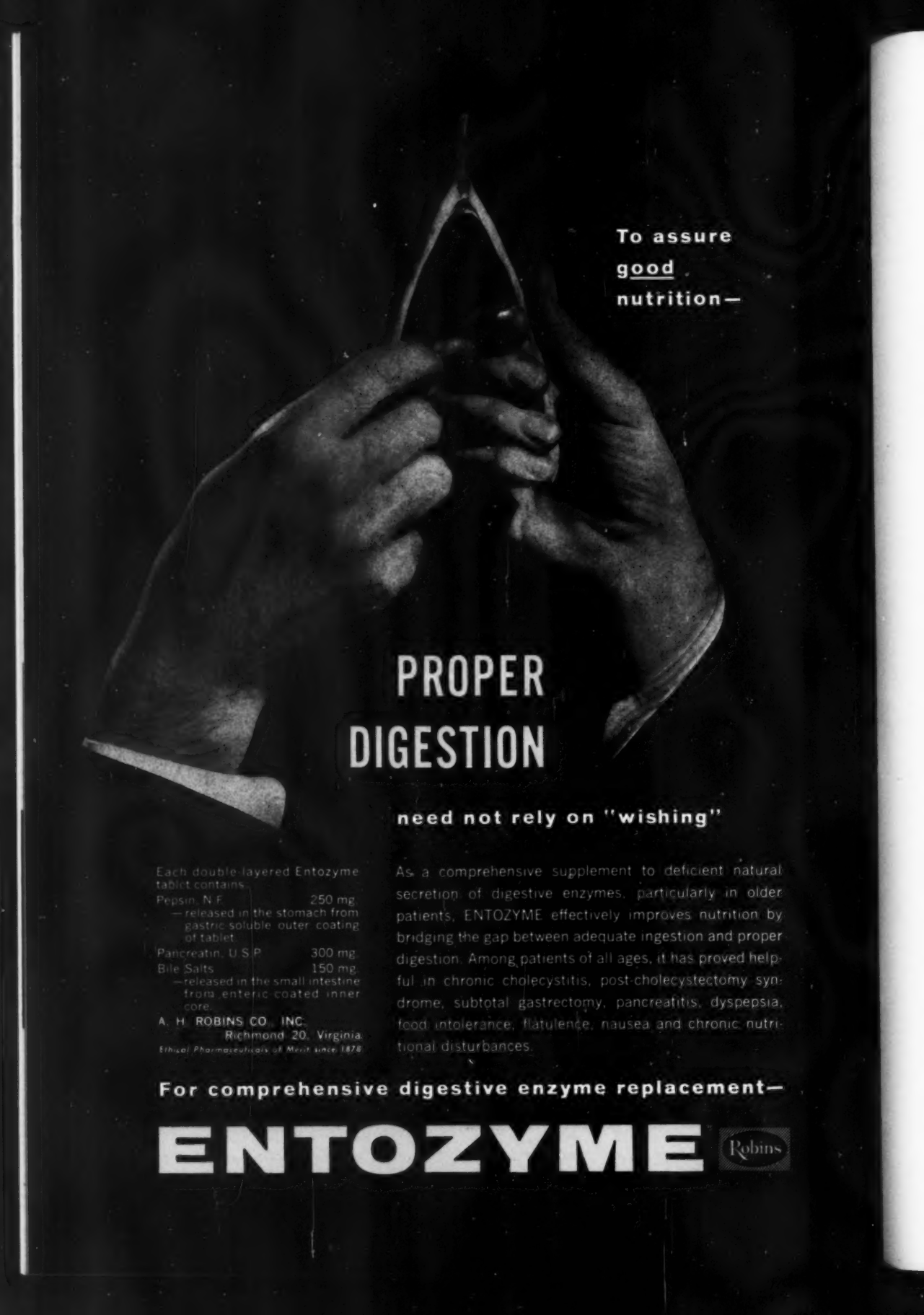

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REFERENCES:
1. Scherbel, A.L., Schachter, S.L., and Harrison, J.W.: *Cleveland Clin. Quart.* 24:93, Apr., 1957.
2. Editorial: *Bull. A. Mil. Dermatologists*, The Shuck Section 5: 25, Nov., 1950.
3. Cornbleet, Theodore: Arch. Dermat. 73:572, June, 1956.

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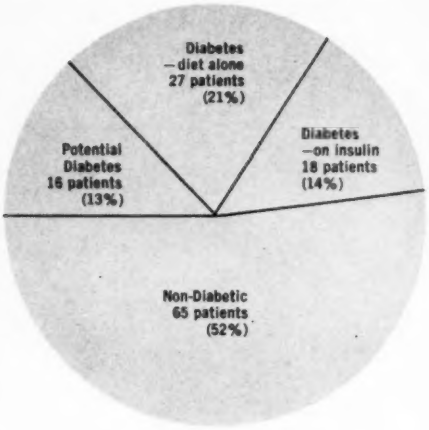

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*Murphy, R.: Connecticut M. J. *21*:306, 1957.

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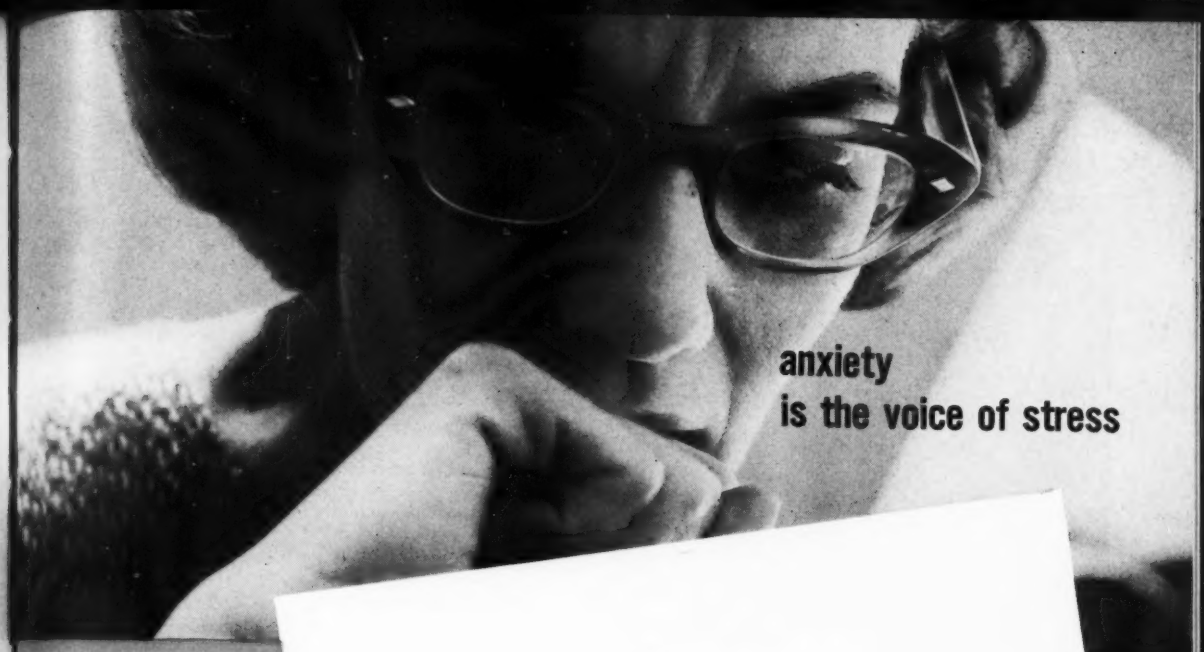

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tension
is a state
of stress

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Continued from page 86

tive Council are: Drs. G. Slaughter Fitz-Hugh, Howard L. Mitchell, L. Benjamin Sheppard, George N. Thrift, Albert R. Gillespie, Albert E. Long, and Peter A. Wallenborn.

The Eye Bank and Sight Conservation Society of Virginia, sponsored by The Lions Clubs of Virginia, was recently established and is located at The Elbyrne G. Gill Eye and Ear Foundation, 711 South Jefferson Street, Roanoke, Virginia.

Dr. Edwin P. Jordan has been awarded a certificate of merit by the National Society for Medical Research "in recognition of vital contributions to public health and welfare made by helping to inform the public of the experimental method underlying the achievements of the biological sciences."

Dr. R. Preston Hawkins, Jr., Clifton Forge, succeeds Dr. J. Earl McIntyre as President of the Association of Surgeons of the C. & O. Railway.

The Clifton Forge Board of Health has elected Dr. G. S. Hartley as its Secretary. He has also been named Health Officer for the City.

The following Virginia physicians have been named as Fellows of the American College of Physicians:

Continued on page 94

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LOCATION AVAILABLE—Excellent location available for physician planning to do eye, ear, nose and throat, Tuscaloosa, Alabama. Office and complete office equipment now available due to death of physician with large established practice. Contact Mrs. A. M. Walker, 15 Forest Lake Drive, Tuscaloosa, Alabama.

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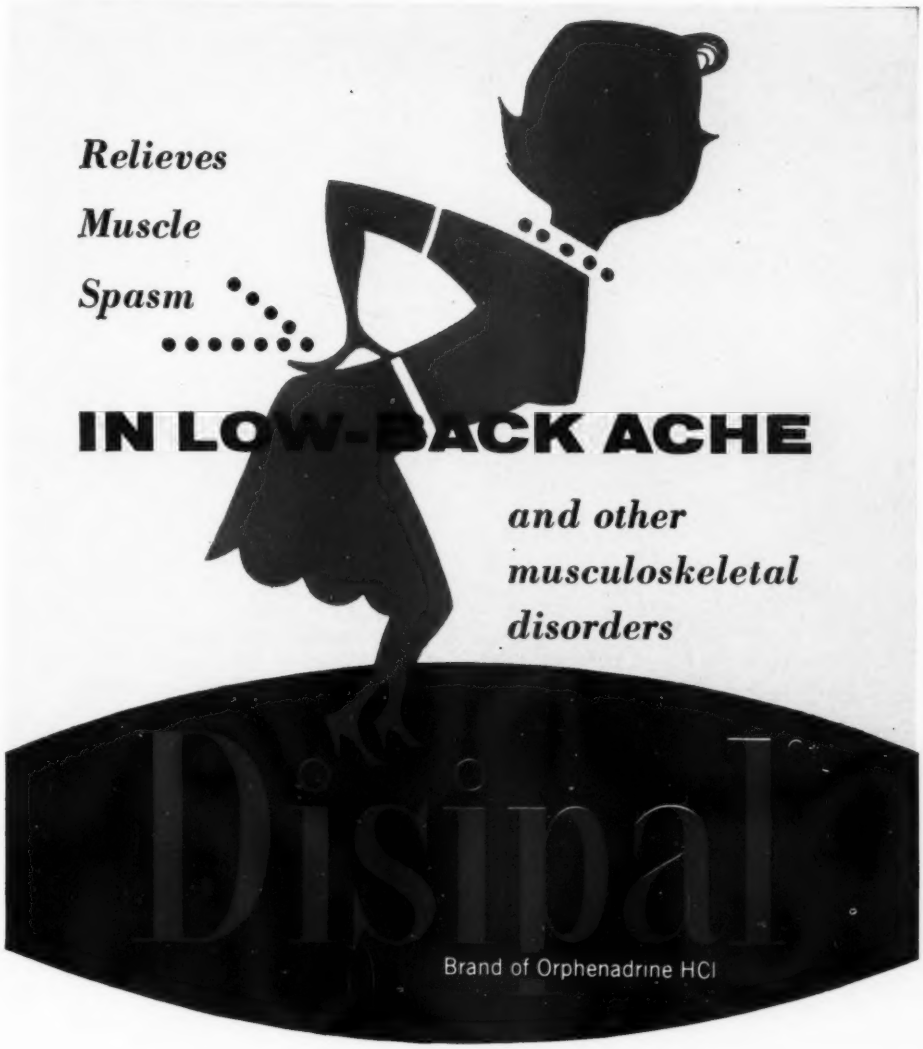

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Continued from page 92

Joseph Davis Lea, Norfolk; Arnold Ferdinand Strauss, Norfolk; and Isabel Taliaferro, Richmond. The following were named as Associates of the College: Joseph Beinstein, Arlington; Leo Ernest Johns, Jr., Norfolk; Arthur Sanford Kaplan, Norfolk; James William Lambdin, Franklin; Paxton Pitman Powers, Staunton; and William Whitfield Regan, Richmond.

Dr. William Philip Wagner has been appointed Director of the Tri-County Health District.

Dr. Harold W. Miller, Woodstock, has been reappointed Medical Examiner of Shenandoah County for another three year term.

Dr. Willard R. Ferguson is the new Health Director for the Dinwiddie District.

The following are new officers of the Medical Society of Virginia: Dr. Harry C. Bates, Jr., Arlington, President; Dr. Walter P. Adams, Norfolk, President-Elect; and Dr. J. R. B. Hutchinson, Arlington, Dr. H. H. Hurt, Lynchburg, and Dr. C. C. Hatfield, Saltville, Vice-Presidents.

WEST VIRGINIA

Dr. Guy R. Post has been named Director of the Marion County Health Department.

Dr. James P. McMullen, Wellsburg, has been named as the recipient of the 1957 Alumni Achievement Award by Bethany College.

Dr. John W. Heson, Jr., has joined the staff of the West Virginia University Health Service.

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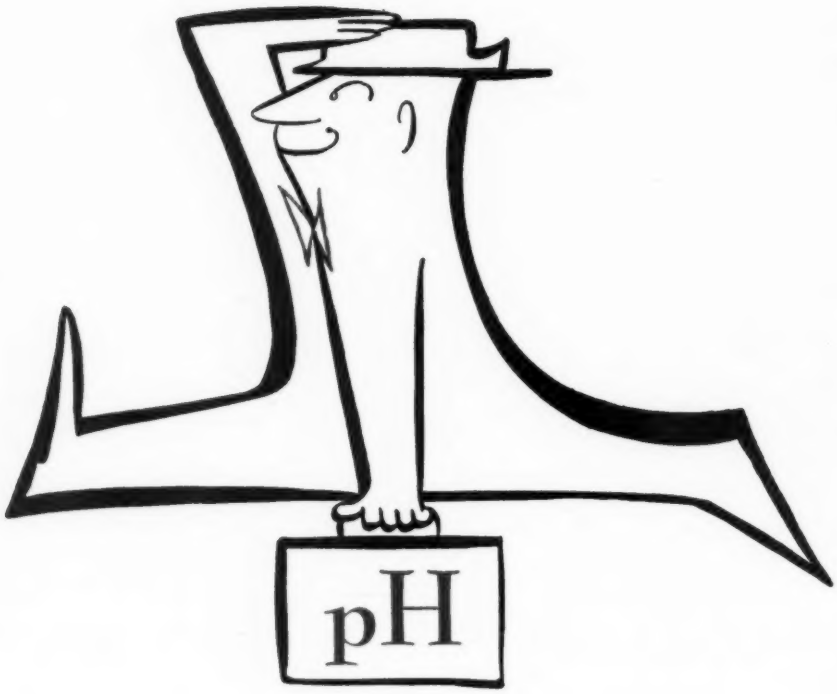

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